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THE ROLE OF THE SURGEON IN THE MANAGEMENT OF PEPTIC ULCER 191
Owen H. Wangensteen

VENOUS THROMBOSIS AND PULMONARY EMBOLISM 196
John Homans

THE SIGNIFICANCE OF EOSINOPHILIA IN ABDOMINAL COMPLAINTS OF AMERICAN SOLDIERS 201
Eric Denhoff

MEDICAL PROGRESS: CANCER 207
Grantley W. Taylor

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL 211

EDITORIALS
Folic Acid 219
Time Out 220

DEPARTMENTS
Miscellany 221
Books Received 221
Notices 222

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SYMBOLS OF SIGNIFICANCE

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Volume 236 FEBRUARY 6, 1947 Number 6

THE ROLE OF THE SURGEON IN THE MANAGEMENT OF PEPTIC ULCER*

OWEN H. WANGENSTEEN, M.D.†

MINNEAPOLIS, MINNESOTA

ULCER is a more frequent cause of discomfort and disability than of death — that is, for every patient who dies, a far larger number suffer. Yet approximately 10,000 people die annually in the United States from ulcer and its complications. There has been no suggestion of improvement in this mortality, such as that in appendicitis and bowel obstruction during the past decade.

GENESIS OF ULCER

Autopsy records indicate that evidence of an ulcer or ulcer scar can be found in 2 to 5 per cent of cases. The observations of William Beaumont[1] on Alexis St. Martin and those of Wolf and Wolff[2] on their subject Tom suggest that gastric erosions occur readily in the stomach. Moreover the observations of Kolouch,[3] of this laboratory, on the exteriorized gastric or intestinal mucosal patch denote that the progress from a mucosal erosion to a fully developed ulcer can occur during the course of a few hours under the influence of dripping of gastric juice on the patch. The causal antecedent of ulcer — mucosal erosion — probably occurs not infrequently in the lives of persons who never develop an ulcer or suffer ulcer symptoms.

The latitude of difference between a patient who develops a clinical ulcer and one in whom ulcer fails to progress beyond the erosion stage is not measurable. Every person whose stomach responds normally to ingestion of food and other stimuli may be a potential ulcer candidate. Resolving the nature of the ulcer diathesis is not an easy matter.

Ulcer, which often develops spontaneously in man, is decidedly unusual in the ordinary laboratory animals, as both Mann[4] and Ivy[5] have been at pains to point out in observations on dogs. The standard laboratory procedure for the production of ulcer in the dog up until recently was the Mann–Williamson[6] procedure of moving the duodenal segment, into which bile and pancreatic juice drain, down to the terminal ileum and thus precluding opportunity for neutralization of the acid gastric juice by the alkaline digestive juices. This disarrangement of Nature's plan obviously is distinctly unphysiologic from many points of view; nevertheless, the method has been of value in focusing notice on the great importance of the acid-peptic factor in the genesis of ulcer. This laboratory has for some time been exploring agencies that abet or accelerate the ulcer diathesis. The placement of histamine in beeswax,[7] from which vehicle the histamine is gradually released, has proved a useful tool in the investigation of items that may favorably influence the ulcer diathesis. By this means alone, ulcer can be produced in most laboratory animals.[8, 9] Moreover, agencies by which the blood supply of the gastric or duodenal mucosa may be altered or impaired appear to favor the development of ulcer. Fractures accompanied by fat embolism may give rise to the spontaneous occurrence of ulcer in man.[10] Fat, injected intravenously into small laboratory animals in small doses, when accompanied by the simultaneous administration of histamine in beeswax, abets and accelerates the development of ulcer. Similarly, anoxic areas produced in the gastric mucosa by the administration of Pitressin or adrenalin favor the development of ulcer.[10] Surprisingly enough, nitroglycerin appears to have the same effect.

TREATMENT

The objective of treatment in conditions that threaten life or make patients miserable is to save life, allay symptoms, re-establish normal function and restore the patients to economic usefulness — by the simplest and most effective means. There are essentially three ways of treating an ulcer. In the first the physician — in this instance a psychiatrist or psychosomaticist — endeavors to talk the patient out of his difficulty. This is obviously the simplest form of therapy, but it remains to be proved, despite the present popularity of the method,

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how permanent the results of such treatment may be. Secondly, the patient is instructed to eat his way out of his troubles — diet. And thirdly, surgery is invoked with the hope that this expedient will ensure a more lasting cure than that achieved by the two preceding agencies.

As a surgeon, it would be presumptuous of me to attempt to discuss any but the last aspect of this problem.

Indications for Operation

In our clinic, 80 per cent of patients undergoing resection for ulcer have had one or more of the conventional complications of ulcer, including perforation, hemorrhage and obstruction. In our experience, the typical patient accepting resection for ulcer is a man in the middle forties whose symptoms trace back fifteen years. Inasmuch as the patients come largely from the rural areas of Minnesota, the typical patient is a farmer whose work should not be especially conducive to the ulcer diathesis. Moreover, I have been unable to observe in these patients any common behavior pattern, which the routine employment of psychiatric technics might uncover; nor can I see any such uniform physical conformation in ulcer patients as was formerly described under the designation "ulcer habitus."

In this clinic, only 2 patients under twenty years of age have undergone resection for ulcer. One was a boy of fourteen who first suffered a severe hemorrhage from a duodenal ulcer at the age of ten. After an interval of four years, during which many such occurrences threatened his life, a three-quarter resection was undertaken in the presence of massive hemorrhage. More than six years have elapsed, and the boy has grown to manhood. There has been no suggestion of recurrence. The other patient was a nineteen-year-old boy with repeated massive hemorrhages from a duodenal ulcer. He too has remained well.

Approximately a dozen patients in their twenties have been subjected to resection for ulcer. Patients in their thirties are more numerous, and a fairly large number first developed symptoms in the sixth or seventh decade of life. Several patients in their eighties have submitted to resection for ulcer because of compelling indications for operation, or because of long continued dissatisfaction with medical management.

Perforation. There can be no disagreement concerning the manner of treatment of perforation. This complication has been an important element in the mortality of ulcer. Yet considerable improvement has resulted from the following methods of dealing with perforated ulcers: the use of unabsorbable (silk) sutures, employing Graham's[11] technic of placement of the sutures; lavage of the peritoneal cavity with copious quantities of physiologic saline solution; and the use of chemotherapy. Whereas the general mortality from acute perforation still hovers around 20 to 25 per cent, in institutions where the above precepts guide the therapy, the mortality is approximately 5 per cent.

Hemorrhage. There is room for considerable improvement in the management of hemorrhage attending ulcer. Allen and Benedict[12] were responsible for persuading American surgeons to operate in an attempt to save the lives of patients suffering from massive hemorrhage. The difficulties relating to the problem are many. The decision whether operation should be undertaken is not easily made. Often, too much time is lost by attempts to replace blood loss that is continuing. When a patient has repeatedly been in shock, he is not a good candidate for operation. Physicians and surgeons would do well to consider operating immediately on patients who have a long history of ulcer with previous hemorrhages. The problem may be difficult on other scores. The diagnosis may be in doubt. Gastric cancer, in the experience of our clinic, is not an infrequent cause of sudden massive hemorrhage. And the technical problem in a duodenal ulcer with a large crater may be extremely difficult. The situation usually demands that the duodenum be cut across to find and arrest the source of hemorrhage; then, there remains the extremely difficult task of obtaining a satisfactory closure of the open duodenum — a problem that may be perplexing, especially in the large supraduodenal ulcer crater with perforation into the hepatoduodenal ligament. A number of studies suggest that the mortality in patients treated medically for massive hemorrhage is in the neighborhood of 10 to 13 per cent.[13] Early resort to surgery will spare the lives of many such patients who will otherwise die from exsanguination. In the patient who presents both obstruction and massive hemorrhage, the indication for early surgery is especially imperative.

In this connection, it is probably not out of place to indicate that, in certain cases, the cause of the bleeding remains occult at operation. On the thesis that such bleeding comes usually from a small mucosal erosion that cannot be felt through the gastric wall, I have resected a number of stomachs for massive hemorrhage. Several of these case histories have been reported in detail elsewhere.[10] The situation of fatal bleeding from a single small mucosal erosion in the stomach is well known to pathologists. The condition may be passed over by the surgeon at operation. In cases of massive loss of blood by vomiting, when the surgeon fails to find a likely source for the difficulty, the possibility of a superficial gastric erosion should not be overlooked.

Moreover, bleeding in portal hypertension may also be amenable to correction by gastric resection. It has been taught that the chief source of bleeding is ruptured esophageal varices. Inasmuch as obstruction of the superior vena cava may also give rise to esophageal varices unaccompanied by hemor-

rhage, may it not be proper to ask whether the primary process is due to acid and peptic erosion rather than to hydrostatic rupture? Already, it has been shown that portal hypertension abets the ulcer diathesis.[10] Furthermore, whereas a three-quarter gastric resection uniformly protects against the histamine-provoked ulcer in the dog, a 90 per cent resection fails to afford consistent protection against such an ulcer in the presence of portal hypertension. Obviously, the intent of gastric resection for hemorrhage in the presence of cirrhosis or thrombophlebitis of the portal or splenic vein, or both, is to prevent death from bleeding and thus to prolong life. The operation does not do away with portal hypertension. An operation approaching a total gastrectomy will, I believe, protect against hemorrhage. If the bleeding is occurring from gastric or duodenal erosion, the operation should be adequate; if esophageal erosions are responsible, the separation of the esophagus from the portal circulation will free the esophageal veins from the increased portal pressure. Moreover, reduction of gastric acidity will diminish the tendency to acid-peptic erosion of the esophageal varices.

Obstruction. The most frequent cause of pyloric obstruction is an occult, sealed ulcer crater with extension into the surrounding tissues — that is, the area of induration accompanying a perforating or perforated ulcer in juxtaposition to the pylorus brings about extrinsic duodenal compression and obstruction. The usual location of such an ulcer crater is the posterior wall, with penetration of the pancreas; often, the perforation is into the hepatoduodenal ligament at the superior border of the duodenum. In my experience, the latter circumstance as a cause of obstruction is far more frequent than intrinsic duodenal stenosis. Spasm and mucosal edema, incident to an ulcer near the pylorus, are phenomena that may cause obstructive symptoms. Persistent or recurrent pyloric obstruction generally occurs through Nature's attempt to halt the extension of the ulcer crater. The repair phenomenon of cicatricial contraction is greater in a penetrated ulcer that has extended through all the coats of the gastric or duodenal wall than in an ulcer that has not penetrated through all the layers of the bowel wall. Patients whose obstruction remains refractory to conservative treatment must be operated on.

Pain. In approximately 20 per cent of patients subjected to gastric resection in our clinic, the major consideration that prompted performance of the operation was failure to control pain satisfactorily by dietary measures. Occasionally, a patient's own dissatisfaction with the dietary strictures, whether arising from a dislike of the monotony of the diet or from inability to work under its conditions, has constituted the main indication for operation.

Dissatisfaction with Medical Cure

Dr. John Fast[14] has just completed a study in our laboratory that strongly suggests the efficacy of the Sippy diet in ulcer management. Five dogs were given 30 mg. of histamine in beeswax daily over a forty-day interval. Meanwhile they were fed the Sippy regimen by a gastrostomy tube from 7 a.m. to 9 p.m. At post-mortem examination, ulcer was not observed in a single animal. The only other measure observed that will protect uniformly against the histamine-provoked ulcer is a three-quarter gastric resection.

In most cases dieting for ulcer is not unlike taking insulin for diabetes. It works so long as the medicine is taken. One of the difficulties, however, is that the gastric mucosa is a sympathetic tissue and responds to diverse stimuli of every sort. Almost anything ingested stimulates gastric secretion. Protein-containing foods possess the greatest capacity of uniting with the hydrochloric acid of the gastric juice, and amino acids appear to be more effective in this respect than native proteins. We have found no substrate, however, that, when fed through an inlying gastric tube, keeps the reaction of the gastric juice in patients with bleeding ulcer consistently above pH 3.5 — the proteolytic end point for pepsin. Arrest of the acid-peptic erosive action of the gastric juice by any agency would be a great boon in the treatment of ulcer, particularly in the management of actively bleeding ulcers.

Nevertheless, dissatisfaction with the dietary management of ulcer is being forcefully expressed. Heuer, Holman and Cooper[15] have reviewed the results of medical and surgical treatment of ulcer at the New York Hospital. They found that approximately 40 per cent of patients have unsatisfactory results from medical treatment. More recently, Krarup[16] reviewed the results of medical treatment of ulcer on Meulengracht's service at the Bispebjerg Hospital in Copenhagen; he observed that the results of treatment were poor in 24 per cent of bleeding and in 43 per cent of nonbleeding ulcers. In patients in whom the duration of ulcer symptoms was longer than a year prior to treatment, the incidence of failure of medical treatment was 32 per cent in bleeding and 45 per cent in nonbleeding ulcers. In patients who had previously undergone one or more medical regimes for ulcer, the incidence of failure was 34 per cent for bleeding and 58 per cent for nonbleeding ulcers. Krarup concluded that in patients whose ulcer distress is of more than a year's duration, and if two medical regimes have been gone through without recovery, the chance of failure of repeated medical treatment is so great that surgical treatment ought to be taken into consideration.

A deterrent, to which careful heed should be given in the protracted conservative management

of any patient with a persistent gastric ulcer, is that the possibility of malignancy cannot be completely excluded. In prepyloric lesions, in particular, this is an important consideration — so important, I believe, that in all patients with such defects the item of malignancy should be carefully weighed. The roentgenologist should appreciate how much the nature of his report determines or influences the course of action in such patients.

Shortcomings of Surgery

Dissatisfaction with the accomplishments of surgery in the ulcer problem is also real. The distrust of internists, actuaries and military authorities in the ability of surgeons to rehabilitate medical failures of ulcer management by surgical treatment is well known. Surgeons, obviously, have been too empirical in their approach to the ulcer problem, endorsing and employing procedures without a clear-cut definition of the criteria of an acceptable operation for ulcer. Let anyone who suggests a new operation for ulcer that is not founded on sound physiologic principles beware of the hazards of premature judgment! The late Lord Moynihan stated that the accomplishments of gastrojejunostomy stamped it as one of the great operations devised by surgeons for the relief of ulcer. What empty words in the light of critical experience!

An Acceptable Operative Procedure

The histamine-in-beeswax technic has proved a useful instrument in defining the criteria of an acceptable operation for ulcer. A three-quarter (75 per cent) gastric resection made with a short afferent duodenal loop affords consistent protection against the histamine-provoked ulcer in dogs when other abetting influences are not employed simultaneously. Gastrojejunostomy and the small gastric resection (less than 50 per cent) fail consistently. The experimental evidence of the necessity of employing a short afferent duodenojejunal loop to protect against recurrent ulcer appears complete. The Billroth I procedure apparently necessitates the same extent of resection (75 per cent) as a satisfactorily performed Billroth II operation to protect against the histamine-provoked ulcer.[10] In man, excision of the antral mucosa is a necessity; failure to remove the mucosa, even despite an otherwise adequate gastric resection, invites a stomal ulcer. Vagotomy also fails to protect against the histamine-provoked ulcer. Inasmuch as histamine acts directly on the parietal cells in the gastric tubules, no such protective action of histamine from vagotomy is perhaps to be anticipated. Hartzell[17] studied the effect of bilateral vagotomy on gastric secretion in the dog. During the five-month interval following operation, Hartzell noted a distinct reduction in the gastric secretory response to ingested meat. Vanzant[18] restudied the remote results of vagotomy in 4 of Hartzell's 8 dogs more than two years after the vagotomies had been done. At that time, Vanzant noted that the depressing effect of vagotomy on gastric secretion had been lost. The cephalic or psychic phase of gastric secretion, which is ablated by vagotomy, may be a vital factor in the spontaneous occurrence of ulcer in man. That the cephalic phase of gastric secretion may be more important in man than in the dog is difficult to believe, when one observes the eagerness of a hungry dog anticipating a piece of meat. In any event, the observations of Dragstedt[19] and his associates will be followed with the keenest interest by all who are concerned with the problem. Vagotomy, however, is not an experiment that should be undertaken simultaneously in many quarters. Dragstedt will be able to determine in reasonable time whether the results in man are abiding.*

Surgical Cure

A successful operation for ulcer must not compromise the future for the patient by holding over him the threat of recurring ulcer. That, in the main, has been the indictment against operations for ulcer; it is a just criticism. A satisfactory operation for ulcer, in addition, in the hands of experienced surgeons, should carry a risk to life that is less than that of the disease for which operative relief is undertaken. Furthermore, it should hold out to the patient relief from distress and from the monotony of dietary strictures. An acceptable operation for ulcer should impose no significant new difficulties on the patient.

It is well known that patients with gastric ulcer are more readily cured of the ulcer diathesis by surgery than patients with duodenal ulcer. Similarly, women appear to be more easily amenable to cure by operation than men, in whom ulcer is far more frequent.

Results of Operation

The experience of this clinic is that gastric resection for ulcer, as described below, can be carried out in elective operations at a risk of 2 or 3 per cent. The over-all mortality, including that in emergency operations for perforation and massive hemorrhage, has been 5 per cent. In more than 500 consecutive patients who have had resections for ulcer performed over an eight-year period, there have been 2 cases of stomal ulcer, both of which occurred in heavy men, short in stature and of stocky, hypersthenic build. Both patients had undergone an earlier gastrojejunostomy for bleeding duodenal ulcer elsewhere. Both patients have severe hypertension. One of them has done well, with a partial return to some of the dietary strictures to which he submitted before operation. I have operated again on the

*In a paper presented before the St. Paul Surgical Society on January 14, 1947, by Dr. Waltman Walters and his associates of the Mayo Clinic, little support was lent to the thesis that vagotomy is a satisfactory primary operation for ulcer. They reported failure of the ulcer to heal following vagotomy, as well as cases of hemorrhage and perforation. Such occurrences do not augur well for the future of vagotomy.

other patient. At the time of the first gastric resection only a small section of stomach (155 gm.), including 6 cm. of jejunum, which was not weighed separately, was removed; if this segment is considered to have weighed 20 gm., a section of stomach weighing only 135 gm. was removed — too small an amount for the usual resection. The primary difficulty is, however, that stout men of hypersthenic build have a short transverse stomach whose fundus lies closely tethered to the left diaphragm and the hilus of the spleen. In other words, in a thin patient whose stomach hangs down in the form of a fish-hook, it is not a difficult task for the surgeon to remove the requisite amount of stomach. In an unobstructed patient, the usual weight of the excised gastric tissue in a three-quarter resection is 175 gm. In patients with obstruction the weights of such excised specimens obviously run considerably higher. In the patient with the recurrent stomal ulcer on whom I reoperated, an additional 86 gm. of gastric tissue was removed. He has remained well.

The policy in our clinic has been to do a one-stage procedure, taking time to do what needs to be done. I see little justification for performing an inadequate operation such as gastrojejunostomy[20] in the difficult cases, electing to perform gastric resection only in those patients in whom it may be performed without difficulty. Moreover, in difficult duodenal ulcers the choice need not lie between a compromise measure, such as gastrojejunostomy with an admitted incidence of stomal ulcer of 15 per cent, and a resection that risks the continuity of the common bile duct and requires a tube in the duct.[21] The antral mucosa can be excised, the pyloroantral muscle cylinder being left. The experience of our clinic is that such an operation can be done with a reasonable risk, and the ultimate promise of success is the same as in the straightforward gastric resection.[22] As a matter of fact, in these difficult operations, performed on somewhat less than 100 patients, there have been no stomal ulcers. The objection to more universal adoption of the pyloric-exclusion operation, with excision of the antral mucosa, has been fear of leakage through the segment with the development of a subphrenic abscess.

The Dumping Syndrome

One of the disturbing items accompanying gastric resection has been the occurrence in some patients of what might be described as the "dumping syndrome," which is frequently observed in all patients soon after operation but persists in a few for long periods. Whether these symptoms are physiologic or psychologic is difficult to determine. Dr. David Gaviser[23] has been at work in this clinic on the problem for some time, and it is hoped that some enlightenment may be shed on its mechanism. Loss of the pyloric sphincter in gastric resection permits quick filling of the jejunal segment, a circumstance against which the pylorus ordinarily affords protection. Sudden dumping of the contents of the stomach into the jejunum may be accompanied by nausea, pain and vomiting. Eating slowly and in small amounts at a time, and the avoidance of drinking with meals, ameliorates the symptoms considerably. In most cases the time factor adjusts the situation satisfactorily. The frequency with which milk and cream are shunned by the ulcer patient after gastric resection suggests that the problem merits investigation.

Moreover, some patients undergoing gastric resection for ulcer, particularly those who were thin prior to operation, manifest some difficulty in maintaining weight. Whether this circumstance is due to difficulty with food ingestion or to absorption is not known. Metabolic studies should be made in a few such patients to determine whether the operation has interfered with the assimilation of protein and fat.* Serious anemia has not been observed after the three-quarter resection for ulcer.

* * *

It is not known whether the margin of difference between a patient having an ulcer and another without ulcer, whose stomach responds normally to extrinsic stimuli, is wide or narrow. No means of measuring this difference have been determined. Whether the difference is qualitative or quantitative and primarily concerns factors of secretion or tissue resistance to acid-peptic erosion is also not known. I am inclined to believe that the latitude of difference between a patient with ulcer and another without ulcer is not great. In other words, patients whose stomachs secrete normally may be tight-rope walkers so far as the ulcer problem is concerned and may, with slight provocation, be catapulted into ulcer difficulties. The great advantage of a slightly superior force is well documented in biology. The lungs are kept expanded by a force that is less than 1 per cent of the major operating force, atmospheric pressure.

Ulcer can be produced by stimulating an animal's endogenous gastric secretory mechanism with histamine. Moreover, agencies that favor the occurrence of anoxic areas in the gastric mucosa encourage the ulcer diathesis.

The three-quarter (75 per cent) gastric resection protects against the ulcer provoked by histamine in beeswax in the dog. Employment of a long afferent duodenojejunal loop in such an anastomosis invites stomal ulcer. Vagotomy fails to protect against the histamine-provoked ulcer in the dog, rabbit and cat. The Sippy diet fed through a gastrostomy tube to dogs receiving histamine in beeswax affords protection against the development of ulcer.

*Wallaeger and his associates at the Mayo Clinic have recently reported carrying out such studies (Forum on Fundamental Surgical Problems, Cleveland, December 19, 1946). They observed unusually large amounts of fat in the stools of some patients who experienced difficulty in maintaining their weight after a Billroth II type of gastric resection for ulcer.

An ulcer operation tested in the experimental laboratory against the powerful capacity of histamine to provoke ulcer in dogs has proved successful for combating the ulcer diathesis in man. The important components of such an operation are extensive gastric resection (75 per cent), employment of a short afferent duodenojejunal loop, a retrocolic anastomosis being made at the suspensory duodenojejunal ligament, and excision of the antral mucosa. Failure on the part of the surgeon to observe all these elements of a satisfactory resection may invite a stomal ulcer. Consistent meeting of these criteria by the surgeon in every gastric resection performed for ulcer will dispel the myth of the intractable ulcer.

Although the prospect of an operation that will preclude recurrent ulcer may be heartening to both patient and surgeon, it is to be hoped that further study will uncover methods of achieving the same end by lesser means. Dispensable as the stomach appears to be, the outlook to ulcer sufferers would be brighter if simpler means were devised to overcome the ulcer diathesis, permitting the patient to keep his stomach intact. Surgeons must continue to be realists, however; wishing-wells are not a solution to the problem. Until a more adequate operation than gastric resection is available, the problem of ulcer must be faced in the light of present knowledge.

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VENOUS THROMBOSIS AND PULMONARY EMBOLISM*

John Homans, M.D.†

BOSTON

PULMONARY embolism, once regarded as an unavoidable accident of surgery, today preoccupies the minds of many clinicians, physicians and surgeons alike. For it is recognized as a threatened complication in the great field of serious diseases, injuries and operations that depress the patient and enforce life in bed.

In the last decade, pathologists have shown that when post-mortem examinations of the legs are thoroughly made, thrombosis is found in the deep veins of the calf in nearly 50 per cent of all cases at autopsy. Much of this thrombosis is terminal and in no sense a cause of death. Yet it fits in with clinical experience in calling attention to a process, relatively frequent in the hospitalized patient, that may readily become a source of embolism.

In the study of thromboembolic disease, it will be convenient to consider first embolism and, secondly, the diagnosis and treatment of venous thrombosis in the lower limbs.

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1946.

†Surgeon emeritus, Peter Bent Brigham Hospital.

Pulmonary Embolism

On the clinical side, pulmonary embolism is being recognized by symptoms and signs often regarded in the past as indications of primary disease of the heart and lungs or perhaps as commonplace complaints having no special significance. Hardly any one sign is, in itself, authoritative. It is the combined evidence from several sources that makes the diagnosis, and although in different clinics — those prevailingly medical or surgical, for example — emphasis is apt to be placed on one or another group of symptoms, the relative significance of the clinical changes pointing to embolism is indicated in the order of the following paragraphs.

Thoracic symptoms and signs may be expected in about 50 per cent or more of all cases. Pain, although not universal, is the most frequent symptom; it usually takes a pleuritic form, being referred to

one side or the other. Yet it may be substernal, with a strong element of distress or gripping. Cough is less specific, perhaps, than pain and is most significant when combined with hemoptysis, which is extremely important if present, although a diagnosis is often made without it. When associated with cardiac failure, it strongly suggests embolism. Shortness of breath is associated with the severer cases of embolism, especially when there is other evidence of right-sided cardiac embarrassment. But although it may lead rapidly to death, its persistence for many hours or even days is not inconsistent with complete recovery. Pulmonary and peripheral congestion, as signs of cardiac failure, are frequently noted in medical cases.

Associated symptoms and signs of thrombosis in the legs are observed with a frequency proportional to the diligence with which they are sought. They are best seen against a background of preliminary routine observations and, since even a bilateral thrombosis is rarely symmetrical, by comparison of one leg with the other. Subjective complaints usually take the form of pain, referred to some part of the calf and, as a rule, accompanied by local tenderness of a deep sort, particularly on the outer, posterior face of the lower leg. Objective signs of thrombosis are related to the state of the great muscles. The earliest are slight increase, by measurement, of the largest diameter of the calf, an increased firmness or elasticity on compression and a tendency to resist dorsiflexion. Signs of venous engorgement are not to be expected in bed patients, but slight cyanosis of the foot may be evident on standing or even on hanging a leg out of bed, and edema, on more prolonged dependency.

An elevation of the pulse rate and temperature — a clue that is especially emphasized by Bauer[1–3] and by Allen and his associates[4, 5] — is most frequently obtained from a surgical chart that has previously leveled off following an operation or injury. It appears to be seen less often in patients with cardiac disorders and other serious illnesses. It may well represent early, preclinical pulmonary embolism.

Circulatory failure of some degree — that is, faintness or actual loss of consciousness — may result reflexly from any infarction. The general circulation may react rather violently to the lodgment of an embolus, and yet may readjust itself within a few hours if no further insult occurs.

Roentgenologic evidence of pulmonary infarction, if obtainable, is of primary importance, as Hampton and Castleman[6, 7] have demonstrated. But the infarct, although entirely characteristic, if a proper exposure can be secured for the x-ray film, shows poorly in plates taken in bed. It is therefore best seen in ambulatory patients deliberately studied; of course, not all emboli cause infarction, owing to the unpredictable efficiency of the collateral pulmonary circulation.

Electrocardiographic signs, which are for the expert, may be pathognomonic, especially soon after the embolus has lodged. Sometimes, exclusion of coronary thrombosis indicates an unsuspected pulmonary embolism.

With such aids to diagnosis in mind, pulmonary embolism can be identified in a surprisingly large number of cases. Undoubtedly, the profession is becoming increasingly alert to its presence. Given a suggestion that embolism has occurred, the slightest sign of thrombosis in the legs is confirmatory. But even without such confirmation, the diagnosis can be made by a study of the nature of the attack or attacks, checked by roentgenologic and cardiographic evidence. Note should, of course, be taken of fatal embolism, but nonfatal forms are more worthy of study.

Phlebothrombosis (Quiet Thrombosis) and Thrombophlebitis

Thrombosis in the veins of the legs should not be regarded as too mysterious a disease. Unfortunately, like many other disorders, it was first recognized in its late, advanced stage — in this case, the unmistakable state of venous obstruction, familiar to all as phlebitis or phlegmasia alba dolens. This outspoken state should, for the moment, be forgotten or regarded as an end-result, a thrombotic occlusion of the femoral and iliac veins. It carries a threat of many disagreeable aftereffects but little danger of embolism. It is rather on the early quiet or bland stage, from which Bauer,[1–3] by phlebographic studies, has proved that it develops, that one should concentrate. This Ochsner[8] has called "phlebothrombosis."

I can do no better than quote from an address of Dr. Lewis A. Conner,[9] in which he recalls his experiences of many years ago with the thrombophlebitis of typhoid fever:

> *It was found that, by careful daily examinations of the lower extremities of every typhoid patient throughout the course of the disease, it was possible to recognize a beginning thrombosis, often many days before the classic symptoms of femoral thrombophlebitis appeared, and to recognize also many minor forms of thrombosis that never, at any time, developed the picture of phlegmasia alba dolens.*

He found pain and soreness on stretching of the calf muscles, a small area of tenderness or, less often, tenderness and induration about the heel and deep in the sole. Following the discovery of such signs, phlegmasia alba dolens might develop in several days to several weeks.

Today's observations have added something. In patients who are to be particularly observed, the calves and ankles are carefully measured — the smallest circumference at the ankle and the largest in the swell of the calf are sufficient — before they undergo the experience, operative or other, that it is thought may lead to a lower-leg thrombosis; special attention should be given to patients over fifty years of age. Each day these observations are

repeated. Instead of feeling soft and relaxed, one calf may seem slightly more firm to the grip of the fingers and may prove to be somewhat larger than the other. The muscles may be somewhat irritable, a state brought out by putting the posterior group on the stretch. Deep tenderness may be present along the course of one of the major vessels or perhaps in the popliteal space. But it should be remembered that among the great muscles of the lower leg there are plexuses of veins in great ladder-like systems, in which thrombosis can be tucked quietly away, giving no signs until it becomes so extensive as to occasion discomfort or provoke resistance when the muscles are squeezed or stretched, or until it reaches the popliteal vein, where it may sufficiently obstruct the blood flow to cause edema and cyanosis of the ankle and foot. Yet even these latter signs need not be seen in the patient entirely confined to bed.

A useful proof of deep thrombosis, insufficiently appreciated, is the presence of a thrombosed area in a superficial vein, particularly on the back of the calf. The hardened stretch of vein is all the more noticeable, as a rule, because no varicosity is present as an excuse for a local thrombus. Such a thrombosed vessel is often part of the lesser saphenous system, which communicates freely with the fibular (peroneal) vessels.

It cannot be too strongly emphasized that the more silent and insidious the deep thrombosis, the more dangerous it is, and the more outspoken, the less liable to cause embolism. In a bilateral disease, for example, when one leg is tensely swollen and the other seemingly normal, embolism is threatened less by the swollen limb than by the apparently innocent one. But although any one thrombosis may have more of an inflammatory character, as marked by pain and soreness, than another, all tend to advance in the end toward a femoroiliac obstruction. Death, in the early stage, will occasionally occur, or the thrombosis may progress so slowly that it permits a current, of a sort, to pass it for a long time. Basically, there is no true distinction between a quiet thrombosis or phlebothrombosis and the familiar thrombophlebitis, although treatment of the two is somewhat different, and since I am dealing with the thromboembolic problem, I shall devote myself to the quiet, early stage of the disease.

Treatment of Thromboembolic Disease

It would be ideal if, in every case of early, deep venous thrombosis, the likelihood of embolism could be known — if, for example, one could say that among 100 cases of thrombosis in the lower leg, 10 to 20 were likely to develop embolism and again, that among the 10 to 20 cases of embolism 3 to 5 would be fatal. Such figures are, perhaps, not far from the facts, but from different clinics come various percentages. Among the general run of postoperative patients, one may expect a lower incidence of thrombosis and embolism than is observed in a group that includes cardiac, prostatic and other extremely ill and elderly persons. Moreover, the diagnosis of venous thrombosis is still so little standardized that consistent figures should not be expected. Again, the age grouping is most important, since embolism, and especially fatal embolism, begins to be seriously threatened only in late middle and advanced age. One had best recognize that in patients committed to bed by operation, accident and serious illness, thrombosis may be encountered so often that it must always be kept in mind, and one should expect embolism, in a mild or serious form, to occur fairly frequently in the early stage of thrombosis. Prophylactic and definitive treatment are based on these considerations.

Prophylactic Treatment

At various times, an astonishing variety of proposals for preventing venous thrombosis in surgical cases has been made, from deep breathing to the giving of dried thyroid gland. Obviously, the first consideration is that the normal activities of the patient should be interrupted as little as possible or, if interrupted, should rapidly be resumed. The term "early ambulation" includes everything intended to restore physiologic normalcy. It cannot be fully protective, since quiet thrombosis may occur without known cause in everyday life, even in young people. Moreover, the very nature of the disease, operation or injury may enforce considerable immobility. Nevertheless, heart disease, most fractures and all surgical operations are now treated with far less confinement to bed than formerly. Above all, the sitting or reclining position in bed, while the legs are relaxed, is to be avoided. And as often as possible the legs must actively be exercised, preferably in elevation, with the aid of an attendant, but if such aid is not at hand, by voluntary contraction and relaxation of muscles, by wiggling of the toes and by describing a circle with the forefoot.

Elevation of the foot of the bed favors a return circulation and avoids venous stasis. Combined with exercise in bed, this procedure has a favorable influence on thrombosis already established. It should therefore be useful as a preventive measure.

Anticoagulants. The nature of these chemicals is undoubtedly well known. Heparin, an expensive preparation, acts directly on the blood, delaying coagulation. Its effect is noted by the degree to which the clotting time is prolonged, and since it is rapidly eliminated, the drug must frequently be introduced. Even when administered by continuous intravenous drip, as was done at first both by Murray[10] and by Crafoord,[11] it cannot be said to produce an ideal, steadily maintained delay of coagulation for fifteen to twenty minutes (by bedside tests). Actually, it has since been given

almost as successfully by the Swedish school, in divided doses, three or four times a day. And recently Loewe[12] has shown that reasonably good results can be secured by introducing it intramuscularly in Pitkin's menstruum. Dicumarol, the newer anticoagulant, acts on the liver to prevent prothrombin formation. Being inexpensive and effectively absorbed when taken by mouth, it is tending to displace heparin. Its successful use at the Mayo Clinic is reported by Barker, Cromer, Hurn and Waugh.[13] Its dosage, however, is almost more difficult to gauge. The same dose in one patient may lower the prothrombin percentage (prolong the prothrombin time) dangerously, provoking hemorrhage from the intestinal or genitourinary tract or causing excessive arterial oozing following a surgical operation, and yet in another patient may cause no appreciable change in the prothrombin level. Its administration requires experience, skill and daily laboratory analysis of the blood.

Of the two drugs, dicumarol more urgently demands hospital care. Since its withdrawal leads to no immediate restoration of prothrombin, vigorous administration of hykinone (artificial vitamin K) is called for if serious hemorrhage is present or threatened.

With such considerations in mind, the anticoagulants may profitably be used as follows: postoperatively for patients over fifty years of age, when no second-stage procedure is contemplated, especially for those subjected to serious abdominal and pelvic operations, but heparin should not be given within seventy-two hours of the operation nor dicumarol within perhaps forty-eight hours — doubtless, the postoperative uncontrolled period should vary in length with the nature of the operative field; for coronary thrombosis, not only for their effect in preventing the thrombosis in the legs incidental to enfeeblement and confinement to bed but also for their favorable influence on thrombosis in the heart's wall and within its chambers. Wright[14] reports favorably on such treatment.

Vein interruption. Bilateral femoral-vein ligation or section can be recommended for prophylactic purposes in patients over fifty years of age as a preparation for operation in cases of cancer, prostatism and other serious diseases, particularly when a several-stage operation is contemplated, and in the treatment of fractures of the lower limbs requiring immobilization and prolonged treatment, particularly in the affected leg. The femoral vein should be sectioned distal to the profunda branch. For Allen and his associates[4, 5] find that, at this level, protection against embolism is obtained without noticeable disturbance of the venous return.

Definitive Treatment

One can obtain encouraging evidence in favor of either operative or anticoagulant therapy according to different groups of clinicians. At present, the trend of medical opinion seems to favor the anticoagulants, but surgical interruption of the venous tree, at one level or another, has a fascinating definiteness that is brought out in the reports from certain hospital centers. I shall attempt to present the problem from several points of view.

Anticoagulants. Bauer[1–3] and others of the Swedish school, basing their opinion mainly on postoperative and traumatic cases, hold that heparin, given only on the establishment of an early diagnosis of lower-leg thrombosis by methods that include phlebography, is remarkably effective in controlling not only the local process but also any embolism that may already have occurred. Heparin is given intravenously, in separate doses of 150 mg. or less, at regular intervals, without laboratory examinations of the blood. All who have studied their work have been greatly impressed. The Swedish Government furnishes the heparin at a minimal charge — a most important consideration. Recently, dicumarol has been taken up. In the United States this drug is displacing heparin, partly because of its relative cheapness but also because of its greater ease of administration. Whether the intramuscular or subcutaneous use of a menstruum from which heparin can slowly be absorbed will make the older drug as generally acceptable as dicumarol remains to be seen.

Those who believe in treating established venous thrombosis by anticoagulant therapy use it whether or not pulmonary embolism has already occurred, holding that it controls further detachment of thrombus and also prevents thrombosis secondary to the presence of emboli in the pulmonary vessels, favoring healing of the infarct in the lung. Evidently, anticoagulants do not always dispose successfully of the soft, insecure, propagating thrombi in the veins of the lower limb, since fatal embolism has been known to occur on their withdrawal and even during their administration. They appear, however, to render harmless and to heal the thromboses that have not as yet caused embolism, particularly when the process seems to be confined to the lower leg. Thus, they should, and probably do, prevent the extension of many thrombi into the popliteal and femoral veins, preserving the useful valves of those vessels.

Anticoagulants, then, may properly be preferred in the treatment of established thrombosis, when laboratory facilities are available and when the conditions calling for treatment are neither continuing nor recurrent, in thrombosis occurring in active life, in early postoperative and post-partum processes apparently confined to the lower leg and in thrombosis associated with any severe brief illness including coronary infarction.

When embolism has already occurred at any stage of thrombosis, the anticoagulants may still be used, although surgical interruption is probably to be preferred, as pointed out below.

Surgical interruption of veins. This method, decidedly favored in this part of the country, has a most attractive quality in that, if ideally performed, it ends all danger of embolism. Its success depends greatly on early diagnosis and exact localization of the thrombus. A distinct advantage is the ease with which the upper femoral vein can be reached under procaine infiltration, so that a general anesthetic is avoided. A disadvantage is the resulting rather sudden venous obstruction at what may be called the common femoral bottleneck, especially when many deep veins in the lower leg and thigh are already more or less occluded by thrombosis. Then, the collateral pathways, adequate in early, local thrombosis, are decidedly insufficient. Yet if the femoral vein is ligated below (distal to) the great branch entering from among the muscles of the thigh (profunda), thrombosis may, although rarely, to be sure, short-circuit the obstruction with a fatal result. Anticoagulants may be combined with a superficial femoral section to prevent such an accident, although a period of several days must obviously elapse after the operation before the drugs can be administered. Another disadvantage, which is true of every femoral-vein section for established thrombosis, is that the operation throws out of function the important valvular system of the femoral vein, whether or not the process has already occupied that vein. Thus, even if a thrombus in the calf heals without extension, a considerable readjustment of the venous circulation is required. Actually, in some cases, the local thrombus seems to spread following femoral-vein section, increasing muscular irritability in the lower leg and enforcing a minutely governed and rather prolonged convalescence — a matter too seldom realized by either patients or surgeons.

In spite of such objections as the above, bilateral interruption of the femoral vein should be performed in all cases when anticoagulants cannot be given with proper controls and is a preferred alternative to the use of anticoagulants when thrombosis has advanced into the thigh (as shown by local signs and a considerable duration of the disease), especially when embolism has already occurred. This second indication applies to a great group of cardiac patients, bad fractures in the elderly and postoperative cases in general.

As for the level at which the femoral vein is sectioned, the common femoral vessel, proximal to the profunda, for reasons already explained, must be preferred. Into this large vessel a smooth glass tube can be introduced to suck out detachable thrombus. In this way, even the common iliac vein can often be cleared.

Those who believe in performing this operation, even when an obstructive thrombophlebitis is present, hold that the extraction of thrombus from the obstructed and inflamed vein not only lessens such danger of embolism as may exist but also acts favorably, much as does sympathetic lumbar block by procaine, on the secondary vasoconstriction that causes so much discomfort and edema. This point is perhaps well taken, — although the advocates of lumbar sympathetic block maintain that the considerable surgical procedure was unnecessary, — but in any event femoral exploration and section prevent recanalization of the disabled femoral vein and encourage from the beginning a collateral circulation.

Higher interruptions — of the common iliac veins or vena cava — are sometimes desirable. Ligation of the common iliac vein should be used for recurrent or persistent processes believed to be confined to one leg. I[15] have elsewhere given reasons for holding that it offers a collateral circulation decidedly better than is permitted by a common femoral interruption. The approach to both common iliac vessels is extraperitoneal, requiring a general anesthetic, and is sometimes difficult, especially on the left.

Ligation of the vena cava is a last resort in the presence of otherwise uncontrollable embolism, especially when the causal thrombosis is bilateral or unlocalizable. Although statements to the contrary are often made, the operation is one requiring great experience and skill in approaching and handling large blood vessels. At times, it must be accepted as superior in effectiveness to any other procedure, operative or medicinal.

* * *

This discussion has perhaps left a sense of confusion. Should the anticoagulants or operation be preferred as the ideal treatment for threatened or actual venous thrombosis and for threatened or actual embolism? I recognize that the present trend is toward a greater use of the anticoagulants. How far this tendency will go, I am unable to say. For the moment, I have offered a reasonable scheme for making use of one method or the other, observing that in some circumstances there is a choice between them. On behalf of surgery, I beg that it be employed only when it is fully understood what the particular operative procedure may be expected to accomplish. I urge that the anticoagulants be used only when accurate, routine blood studies are available. Undoubtedly, as experience widens, more definite indications for the use of operative or chemical methods of preventing and treating thrombosis in the veins of the lower limbs will be available.

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THE SIGNIFICANCE OF EOSINOPHILIA IN ABDOMINAL COMPLAINTS OF AMERICAN SOLDIERS

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IN THE Southwest Pacific the characteristics of many tropical diseases acquired by American soldiers differed from those described in textbooks. Medical officers suspected new syndromes, but laboratory personnel were frequently unable to confirm these impressions with routine methods. The lack of specific diagnostic evidence often forced a diagnosis of psychoneurosis. In the course of time, it was possible to evaluate certain criteria and to devise practical technics that were helpful in differentiating the neurotic patients from those with unusual manifestations of the usual tropical diseases. Some of these methods have been described in previous publications. For example, the proper interpretation of chromatin dots and pigmented leukocytes in thick smears stained in an unconventional manner helped confirm the diagnosis of malaria in a substantial number of patients with vague, nonspecific febrile reactions.[1] Attention to the significance of high degrees of eosinophilia aided in establishing a diagnosis of filariasis when clinical criteria were lacking.[2] In a large group of patients with gastrointestinal disorders, controlled studies utilizing practical technics helped differentiate functional from organic disorders.[3, 4] A study of hematologic values clarified the significance of eosinophilia in American soldiers.[5]

After thirty-six months of clinical and laboratory experience in the tropics, the evidence was convincing that high degrees of eosinophilia in American soldiers usually indicated helminthic infections. On the basis of this premise, every case of unexplained eosinophilia was studied intensively. Recently, the records of these patients were reviewed. As a rule they were combat infantrymen hospitalized for vague but incapacitating intestinal complaints. Hookworm ova were found in the majority of cases, and Strongyloides in some. In the latter, examination of duodenal fluid was the only method of diagnosis. The similarity of symptoms between the patients with helminthic infections and others previously studied with anxiety neuroses was striking.

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MATERIAL AND METHODS

A large Army station hospital with thirty-six months' service in the South and Southwest Pacific theaters of operation had a substantial number of patients with high degrees of eosinophilia whose causes were not being determined by routine methods. During 1944–1945 in New Guinea, the medical and laboratory services established an "unexplained eosinophilia ward" to study patients in whom laboratory studies on the respective wards did not clarify the cause for eosinophilia.

Clinical studies. Histories in the form of questionnaires, with special reference to allergic diatheses, systemic complaints and exposure to parasitic infections, were utilized. Physical examinations were detailed and frequent. Special diets were available, and recreational facilities in the hospital were excellent for New Guinea.

Laboratory studies. Detailed analyses of the blood and urine were made. Diagnostic gastric and duodenal intubations, roentgenograms of the gastrointestinal tract, using contrasting mediums, and of other systems when indicated, and proctoscopies were performed routinely on the last 25 patients. Each fecal specimen passed during the first three days was studied for ova and parasites by a concentrated method.[6] Thereafter, at weekly intervals, a dose of magnesium sulfate was administered, and all stools passed on that day were examined. The blood, urine, gastric and duodenal fluid and prostatic secretions were also examined for ova and parasites. An eosinophilia of 9 per cent or more was considered significant. Cutaneous testing materials for specific allergins were not available.

Results

Fifty-nine patients with unexplained eosinophilia were studied. Forty-seven (79 per cent) were found to have intestinal helminthic infections. Of this group, 42 (89 per cent) had hookworm disease, whereas 5 (11 per cent) had strongyloidiasis. In the 12 other cases the cause for the eosinophilia could not be determined.

Table 1. *Pertinent Data in 59 Patients with Eosinophilia.*

Datum	Hookworm Disease* (42 Cases)	Strongyloidiasis† (5 Cases)	Eosinophilia of Undetermined Origin‡ (12 Cases)
	no. of cases	no. of cases	no. of cases
Admission diagnosis:			
Psychoneurosis (abdominal complaints)	11	3	5
Appendicitis	4	–	1
Gastroenteritis	4	1	1
Hookworm disease	3	–	–
Peptic ulcer	3	–	1
Gastritis, acute	2	–	–
Duodenitis, acute	1	–	–
Colitis, acute	1	–	–
Dysentery, acute	–	1	–
Sciatica	1	–	–
Arthritis	1	–	1
Surgical conditions	5	–	–
Malaria	1	–	–
Scrub typhus	2	–	–
Bronchitis	1	–	1
Cephalgia	1	–	–
Hepatitis	1	–	–
Dermatosis	–	–	2
Signs and symptoms:			
Abdominal distress	29	5	7
Anorexia	14	5	8
Nausea	14	1	5
Weakness	13	3	5
Fatigue	13	3	5
Weight loss	12	3	5
Vomiting	10	3	3
Nervousness	10	4	5
Headache	8	1	5
Joint pains	6	–	3
Palpitation	5	–	–
Tremors	3	–	4
Nightmares	3	2	6
Occurrence of symptoms:			
During or after combat	26	4	5
Before combat	4	1	1
On Louisiana maneuvers	1	–	1
Prior to induction	9	–	5
Previous hospital admission for psychoneurosis	10	4	5

*The average onset of symptoms after exposure was one hundred and forty-seven days, the average duration of symptoms before hospitalization was one hundred and thirty days and the diagnosis was made, on the average, eighteen days after admission.

†The average onset of symptoms after exposure was twenty-four days, the average duration of symptoms before hospitalization was one hundred days and the diagnosis was made, on the average, forty-one days after admission.

‡The average duration of symptoms before hospitalization was two years.

The findings in the three groups of patients described are presented in Tables 1 and 2.

Hookworm Disease

Of 42 patients with hookworm disease, 29 (69 per cent) were admitted with diagnoses referable to the gastrointestinal tract, including psychoneurosis, gastroenteritis, appendicitis, peptic ulcer, duodenitis, colitis and hookworm disease. In 2 cases the diagnosis on admission was acute rheumatoid arthritis, and 11 patients were hospitalized for conditions not related to the helminthic infection. The patients were studied because eosinophilia was found on routine blood examination. Ten patients (25 per cent) of the entire group had previously been hospitalized with the same complaints.

The predominant symptom was abdominal distress, which most patients described as an intermittent, severe, cramplike pain in the epigastrium that usually occurred after eating and lasted a few hours. The pain was more intense at night and was not relieved by food, alkalies or defecation. Others complained of dull, aching sensations in the periumbilical region, and a few had inconstant pains in the midabdominal area that radiated to the chest or back. Some patients were disturbed by constipation alternating with soft, mushy movements, although in the majority of cases the bowel habits were normal. Almost all patients emphasized anorexia, nausea, weakness, fatigue, weight loss, vomiting and nervousness. Less frequent complaints were headache, palpitations, tremors and nightmares. Physical examinations were not helpful.

The majority of patients had been sufficiently exposed during combat patrols to acquire hookworm disease. Usually, they had slept on the ground, swum in streams near native villages or eaten unpackaged bread dropped from parachutes. On the average, the onset of symptoms after probable exposure was one hundred and forty-three days, and one hundred and thirty additional days elapsed before symptoms became severe enough to warrant hospitalization. Ordinarily a patient was hospitalized twenty-one days before he was transferred to the ward for study, and the diagnosis was most frequently made during that period.

The average red-cell count was 4,300,000, with a hemoglobin of 87 per cent (Sahli). As a rule, there was a slight leukocytosis, although the eosinophil count was high (9 to 36 per cent). Such high counts were usually found on admission and persisted after discharge. Ova of *Necator americanus* were often found in the feces during the third week of study. Other laboratory findings were irrelevant.

Thirty-three patients received tetrachlorethylene in the prescribed manner.[7] The results of treatment were considered successful in 28 cases, although symptoms in a milder form usually persisted and ova were occasionally found. In the other cases neither the symptoms nor the parasites seemed affected, in spite of several courses of anthelminthic therapy. Nine patients treated with carbon tetrachloride responded in a like manner.

The following cases were typical of the group with hookworm disease.

Case 1. A 30-year-old combat infantryman was admitted to the hospital because of headache, dizziness and nausea of 1 week's duration. On the day before admission he had struck his head accidentally. The admission tag stated, "Discharge quickly — patient is neurotic, with fixations of pain in head and stomach."

Two months before admission, the patient first complained of "sick headaches" followed by sharp, knifelike pain in the midepigastrium occurring daily in the late afternoon and persisting until morning. Nausea was frequent, but vomiting was rare. Neither food nor alkalies relieved the pain. During the following month he became irritable, discontented and nervous. He attended sick call frequently, but medication did not help The accident precipitated admission to the hospital.

Physical examination was essentially negative. Laboratory studies revealed an eosinophil count of 14 per cent. Three stool examinations (concentrated method) were negative for ova.

The patient was transferred for further study to the "eosinophilia ward," where the past history was found to be noncontributory. He had been in the combat zone in New Guinea for 1 year prior to the onset of symptoms, but denied any breach of sanitary precautions. Laboratory studies over a period of 3 weeks were negative; these included several stool examinations and two duodenal intubations. The patient was treated with iron and vitamins and returned to duty, because the symptoms had improved.

Three days later, he was readmitted with severe epigastric distress. Physical examination revealed some spasm and tenderness over the right rectus muscle, but this receded promptly after an enema. Eosinophilia was still present. A second gastrointestinal series and two stool specimens examined a week apart were normal. During the 3rd week, ova of *N. americanus* were found in the feces. Treatment was instituted. The symptoms subsided and the patient returned to duty within 3 weeks.

In this case a diagnosis of hookworm disease was made seven weeks after a careful study had been initiated, and four months after the onset of abdominal complaints. This case illustrates that a long period of observation may be necessary before a diagnosis of hookworm disease can be established.

Case 2. A 22-year-old infantryman was admitted from combat to a field hospital with bronchopneumonia. X-ray examination confirmed the diagnosis, and penicillin was administered. The patient recovered but during the week developed a mild diarrhea. Concomitantly a leukocytosis and an eosinophil count of 11 per cent were found. A stool examination was negative, and the diarrhea receded without specific therapy.

Two weeks later the patient complained of nausea, anorexia and abdominal distress. He was transferred to the hospital with a diagnosis of psychoneurosis. On arrival he was irrational and had hyperactive reflexes. A diagnosis of hysteria was made.

Six weeks later the patient was transferred to the "eosinophilia ward." Questioning revealed that in 1942 he had been hospitalized for a fractured skull. Within the following 6 months he had had two convulsions and several violent temper tantrums. He had been inducted into the Army in January, 1943. In August, while on maneuvers, he had had urticaria and hay fever. En route to New Guinea in May, 1944, he had been operated on for appendicitis. During combat patrols in October, 1944, he had swum in fresh-water streams and eaten native food. He had been sent to rest areas on several occasions but had returned to actual combat of his own volition.

The patient was admitted to the study ward during February, 1945. Physical examination revealed a sullen, uncooperative soldier, who showed evidence of marked weight loss. Laboratory studies revealed a white-cell count of 25,500, with 24 per cent eosinophils. Five stool examinations were negative. A positive diagnosis of hookworm disease was made during the following week. Satisfactory recovery was made after two courses of an anthelminthic.

This case illustrates the difficulties of differentiation. The entire syndrome could have been helminthic in origin, but in view of the previous neuropsychiatric disturbance, it seemed more plausible that the helminthic infection merely precipitated a severe emotional upset.

Table 2. *Laboratory Data in 59 Patients with Eosinophilia.*

Datum	Hookworm Disease	Strongyloidiasis	Eosinophilia of Undetermined Origin
Blood:			
Red-cell count	4,500,000	4,300,000	4,400,000
Hemoglobin (Sahli)	87%	87%	86%
Eosinophil count	9-36%	9-60%	9-33%
Sedimentation rate	Normal	Increased (1 case)	Increased (2 cases)
Sugar	Normal	Normal	Normal
Nonprotein nitrogen	Normal	Normal	Normal
Urea nitrogen	Normal	Normal	Normal
Creatinine	Normal	Normal	Normal
Uric acid	Normal	Normal	Increased (1 case)
Total protein	Normal	Low (1 case)	Normal
Albumin-globulin ratio	Normal	Reversed (1 case)	Normal
Icterus index	Normal	High (1 case)	Normal
Gastric contents:			
Acidity	Normal	Normal	Normal
Microscopical examination	Normal	Larvae (1 case)	Normal
Duodenal contents:			
Appearance	Normal	Mucoid (all cases)	Mucoid (3 cases)
Microscopical examination:			
Epithelial cells and leukocytes	Absent	Increased (all cases)	Increased (3 cases)
Larvae	Absent	Present	Absent
Feces (concentrated specimen):			
Ova	Present	Present (1 case)	Absent
Larvae	Absent	Present (1 case)	Absent
Adult worms	Absent	Absent	Absent
Proctoscopic examination	Normal	Ulcerative colitis (1 case)	Normal
Gastrointestinal x-ray film	Normal	Normal	Pylorospasm (1 case)

Strongyloidiasis

The 5 patients with strongyloidiasis were admitted with the following diagnosis: "Psycho-

neurosis manifested by vague abdominal complaints."

The general pattern of the complaints was similar to that in patients with hookworm disease. There was less specificity, however. Abdominal pain occurred at any time during the day or night, varying in intensity. Often, it was cramplike; it was more frequently described as an "ache that was always there." Other disturbing features were increasing weakness, irritability and nervousness. There was evidence of marked weight loss and asthenia.

Four patients gave adequate histories of possible exposure. The average onset of symptoms was twenty-four days after exposure, but another hundred days elapsed before the distress was severe enough to warrant hospitalization. The patients were hospitalized several months before examination of the duodenal fluid clarified the diagnosis.

The examination of concentrated specimens of duodenal fluid was diagnostic in every case. In 4 patients, motile, rhabditiform larvae of *Strongyloides stercoralis* were found only in the duodenal juice, whereas in 1 larvae were also found later in a diarrheal stool. The appearance of the duodenal contents suggested chronic inflammation. There were large amounts of columnar epithelium and mucous shreds, as well as many round cells, neutrophils, eosinophils and erythrocytes. In 4 cases examinations of the feces were consistently negative.

Treatment consisted of 25 cc. of a 1 per cent aqueous solution of gentian violet, administered intraduodenally. The symptoms persisted in spite of repeated treatment, although 1 patient improved temporarily. The following cases were characteristic.

Case 3. A 28-year-old combat infantryman was admitted with the diagnosis of "psychoneurosis manifested by vague intestinal pains" in July, 1944. While on combat patrol, 7 weeks previously, he had been seized with severe aching cramps across the epigastrium. Nausea, vomiting and diarrhea were conspicuously absent. Because of recurrent attacks, the patient was admitted to a field hospital, where examination, including a gastrointestinal x-ray series with contrasting mediums, was negative. After 3 weeks he was evacuated to this hospital for psychiatric evaluation.

Physical examination showed the patient to be ill and emaciated, with a peculiar gray pallor. Routine studies were negative except for a moderate leukocytosis and an eosinophil count of 35 per cent.

The patient was transferred to the study ward, where questioning revealed that he had been in combat in the Solomon Islands in 1943, with no sequelae. While on combat patrol in New Guinea during the following summer, he had swum in a stream adjacent to a native village and had eaten native food and unpackaged bread dropped by parachute. Detailed laboratory studies during October and December, 1944, had been negative, as were many stool examinations. During the 3rd month of study the duodenal fluid was examined. On the first specimen 8 to 12 actively motile larvae within clear refractile shells (*S. stercoralis*) were found. A large number of columnar epithelial cells, mucous shreds, round cells and neutrophilic and eosinophilic leukocytes were also observed. Specific treatment was initiated, with some relief in the following week. During the 3rd week the symptoms returned in a milder form. Duodenal intubation was repeated. Larvae were not found in the fluid, but a moderate amount of exudate was present. Treatment was repeated, but abdominal unrest persisted. The patient was returned to the United States for further study.

This case demonstrates that negative stool examinations cannot eliminate the possibility of helminthic infections. This patient was hospitalized much longer than usual, because the medical officer was impressed by his complaints. Duodenal intubation clarified the reason for the eosinophilia, and a diagnosis of psychoneurosis was averted. It is possible that a neurosis was acquired during the long period of hospitalization.

Case 4. A 23-year-old combat infantryman was transferred from a field hospital with a diagnosis of "psychoneurosis manifested by vague abdominal complaints." During May, 1944, while on combat patrol, he had noticed constant, needle-like pain in the right epigastrium that was temporarily relieved by food. At night, the pain was intense, but vomiting followed eating. The patient was hospitalized and treated with antispasmodics, returning to duty in 2 weeks. He was readmitted 2 months later because the symptoms were worse. During the interim he had lost 40 pounds of weight and had become extremely nervous. He was transferred to this hospital in September, 1944. Routine examinations were negative except for a moderate leukocytosis and an eosinophil count of 50 per cent.

The patient was transferred to the "eosinophilia ward." During combat in 1942, he had been hospitalized twice for projectile vomiting. Later, in Australia, a diagnosis of psychoneurosis was made. When he returned to combat in May, 1944, he admitted breaches in sanitary precautions.

Three months after readmission examination of the duodenal contents revealed a few actively motile rhabditiform larvae of *S. stercoralis* in each specimen. There was a large amount of epithelial debris and cellular exudate. Eosinophils were abundant. The symptoms persisted in spite of adequate therapy, although larvae were not found again. Evacuation to the United States seemed indicated.

This case also demonstrates the difficulty in differentiating neurotic complaints from symptoms caused by helminths. The past history suggested that the patient was neurotic. The high degree of eosinophilia, however, was a diagnostic lead, and proves that this finding is significant. Again, an unstable personality may explain why complete regression of symptoms was not achieved.

Eosinophilia of Undetermined Origin

In 12 cases no cause for the eosinophilia was found. The symptoms in 9 simulated those in the soldiers with helminthic diseases. All patients had a history of possible exposure, and many had previously been hospitalized for the same complaints. Three patients had histories of allergies and nonspecific complaints that predated Army service.

Laboratory studies were negative, although the duodenal contents in 3 of 9 cases resembled those in which *S. stercoralis* had been found, except that larvae were absent.

Case 5. A 22-year-old infantryman was admitted with a diagnosis of "psychoneurosis manifested by vague intestinal symptoms." The main difficulty was eructation of sour material after every meal. This symptom had begun in 1943, shortly before overseas assignment. In September, 1944, in New Guinea, the patient was hospitalized for gastritis and hepatitis. Because of the persistence of eructations and of a throbbing ache in the epigastrium, he was evacuated to this hospital. Physical examination was essentially negative, but laboratory studies revealed an eosinophil count of 36 per cent.

The patient was transferred to the study ward. He was a native of Mississippi. He had always been allergic to tomatoes

and poison ivy. During combat patrol, in August, 1944, he had bloody dysentery. Laboratory studies revealed an eosinophil count of 32 per cent, and two examinations of the duodenal fluid revealed a marked epithelial exudate associated with neutrophilic and eosinophilic polymorphonuclear leukocytes. No ova or parasites were found. The patient was treated with iron and vitamins. The symptoms improved, and the eosinophil count receded to 12 per cent. He returned to duty 3 months later, when he was somewhat improved.

This case represents a diagnostic problem. The patient had always lived in a region where hookworm was endemic; he had a history of allergy, as well as gastrointestinal symptoms, that predated tropical service, and was convalescing from infectious hepatitis. Clinically, this patient resembled those in cases with strongyloidiasis, and the duodenal fluid simulated the fluid of patients with that finding. Yet, in the absence of larvae, this finding is of questionable significance.

Case 6. A 20-year-old noncombatant soldier was admitted to the hospital with a diagnosis of "generalized myositis." He complained of a stiff neck and aching legs of 2 months' duration. Physical examination revealed a thin, asthenic man, who held his head stiffly to one side. The right sternomastoid muscle was spastic and tender to palpation. Laboratory studies were essentially negative except for an eosinophil count of 28 per cent.

The patient was transferred to the study ward. He had been born and had lived on a farm in Missouri. Ever since childhood the legs had ached and the joints had occasionally swelled. Since induction into the Army he had complained of myalgia on several occasions, and during his overseas service he had been hospitalized with that complaint three times in 3 months. Roentgenograms of the muscles were negative for calcifications. An elevated blood uric acid was found on two occasions, but other laboratory studies were negative. The eosinophil count receded to 11 per cent without specific treatment. The patient was returned to the United States unimproved.

Cutaneous tests for specific allergins, especially tests for trichina, might have clarified the diagnosis in this case. Clinically, the patient had rheumatoid arthritis. He could not be classified as having hookworm disease or strongyloidiasis.

Discussion

Hookworm disease acquired in the Southwest Pacific differs materially from the disease as it is known in the southern United States. It seems likely that the symptoms reflect allergic or invasive phenomena rather than anemia, which is often responsible for the classic manifestations. The fact that it was frequently impossible to find ova in the feces during a period when the symptoms were most distressing strengthens this impression. Allen[8] reported that eosinophilia was present in soldiers long before hookworm ova could be found. Eggs were found, however, when the patients were studied long enough. This was also observed in the majority of the cases discussed herein.

Chacon[9] described early symptoms of ankylostomiasis in Porto Ricans. Violent headaches and dizziness were most frequent initial complaints. Pain in the knees and waist, fatigue, sleepiness and palpitation appeared early in the disease. Three other symptoms were consistently present: epigastric pain, — as well as a feeling of fullness after meals, — mild diarrhea and "watering of the mouth." Soldiers in New Guinea had comparable complaints. Recently, Rogers and Dammin[10] reported a syndrome occurring in American soldiers stationed in Assam and Burma characterized by acute gastrointestinal symptoms, severe diarrhea and eosinophilia. No difficulty in finding hookworm ova in the feces was encountered, however, when specimens were prepared by a flotation centrifugation method. In addition, gastrointestinal roentgenograms showed peculiar cogwheel abnormalities of the small intestine. It appears that the cases discussed above and those reported by Allen represented minimal infestations, whereas those reported by Rogers and Dammin indicated either a heavier parasitemia or an extreme response to the allergin.

Eosinophilia is a most important diagnostic lead in obscure parasitic infections. Although it must be interpreted as a nonspecific finding associated with a multiplicity of allergic diseases, an increasing eosinophilic leukocytosis usually indicates helminthic infection. Similarly, when high eosinophil counts (9 per cent or more) are consistently associated with dengue, scrub typhus, infectious hepatitis, malaria, the dermatoses and the allergic respiratory diseases, in which a value of 6 per cent is average, nematode infection should be suspected. Eosinophilia, which is usually present weeks before the parasite can be demonstrated, generally persists long after treatment has been considered adequate. In the absence of specific cutaneous tests for allergins, eosinophilia must be regarded seriously.

The patients with strongyloidiasis presented interesting diagnostic problems. They were shunted from hospital to hospital, being considered psychoneurotic. They remained on the wards for weeks, obviously ill, but without presenting any positive diagnostic criteria other than eosinophilia. Finally, when the duodenal fluid was examined, motile larvae were found without difficulty. Yet stool examinations repeatedly failed to reveal the larvae, even when they were known to be present in the duodenum. Perhaps, in minimal infections, the parasites are not irritating enough to cause diarrhea. It is usually in that type of stool that the larvae are found.

Duodenal intubation as a diagnostic method in strongyloidiasis has not been stressed sufficiently. It is not a difficult procedure,[11] but it takes time. Fluoroscopy speeds the operation but is not essential. Normally, the alkaline duodenal fluid is devoid of parasites, evidence of an inflammatory reaction or a significant amount of tissue debris. *N. americanus* and *S. stercoralis*, after they have completed their invasive cycle, settle in the small intestine, where their eggs are laid. In addition to fecundity, the worms are said to liberate toxins that cause disturbing nonspecific and gastrointestinal symptoms. Whereas hookworm ova hatch in the feces outside

the body, the eggs of Strongyloides hatch in the small intestine, causing a catarrhal inflammation characterized by a round-cell and eosinophilic exudate.[12, 13] Usually, a persistent diarrhea results in which free motile rhabditiform larvae may be found.

An eosinophilic exudate has been observed in the duodenal fluid in strongyloidiasis but not in that from patients suffering from hookworm disease. Neither the hookworm adult nor ova could be found in the duodenum even at a period when it was not yet found in the feces. In some cases in which eosinophilia remained unexplained, the duodenal fluid suggested an allergic exudate. The significance of inflammatory reactions, however, as portrayed by the duodenal juices, must be regarded with caution, because comparable exudates have been observed following the ingestion of magnesium sulfate.[14]

During this hospital's period of service a substantial number of cases were diagnosed as psychoneurosis. A significant number with the syndrome described in this paper fell into that category. Their symptoms may have been essentially helminthic in origin, but on the other hand, the conditions of jungle warfare may have been responsible for the display of neurotic tendencies. Certainly, long periods of medical treatment without relief or even proper diagnosis contributed to puzzling complaints. The consensus was that these patients were neurotic regardless of their infections. Because treatment was unsatisfactory, as manifested by the persistence of ova or larvae and eosinophilia after adequate anthelminthic therapy, perhaps a definite opinion of the mental reactions should be held in abeyance until additional reports of the early manifestations of helminthic diseases are collected.

Certain criteria that Rush[3] established in a group of patients with anxiety neurosis studied in this hospital help differentiate the true psychoneurotic patients from those with pathologic findings to account for their complaints. The symptoms manifested by Rush's group hardly differed from those in patients with helminthic disease, and yet the type of patient differed. The true neurotic patient had been in the tropics only a short time before he was hospitalized; he was never in combat because he was "always weeded out"; his chief complaint was abdominal pain, which was frequently relieved after defecation; he overaccentuated any single complaint, and this varied from day to day; he showed no evidence of weight loss or malnutrition; and, finally, intestinal parasites were never found, nor was there an eosinophilia. On the other hand, patients with proved or suspected helminthic diseases, who seemed of a different temperament, were consistent in their complaints. Positive or suggestive laboratory findings were always present.

Prior to this study, the causes were found in approximately 40 per cent of soldiers with eosinophilia admitted to the hospital. With special efforts, the reasons for eosinophilia in the majority of cases were clarified. It was gratifying that a diagnosis of psychoneurosis was deferred in a substantial number. Although neurotic tendencies were outstanding in many of the patients studied, evidence is now being accrued that the early symptoms of helminthic infections were different from those that were expected.

Summary

Fifty-nine American soldiers hospitalized in New Guinea were studied for unexplained eosinophilia. Forty-seven (79 per cent) were found to have intestinal helminthic infections. Forty-two (71 per cent) had hookworm disease, 5 (8 per cent) had strongyloidiasis and 12 (20 per cent) presented no demonstrable cause for the eosinophilia.

The majority of patients were admitted to the hospital because of abdominal complaints. A substantial number were classified as psychoneurotic prior to study. The predominant symptom was intermittent, cramplike epigastric pain. Anorexia, nausea, vomiting, weakness, fatigue, nervousness and weight loss were prominent. Physical examination was negative.

The onset of symptoms usually occurred four and a half months after probable exposure, and the symptoms became severe enough to warrant hospitalization during the next four and a half months.

Laboratory studies revealed a persistently high eosinophil count (9 per cent or more). In patients with hookworm disease, ova were found in the feces, usually during the third week of the study. Examination of duodenal fluid was the only method of diagnosing 4 of 5 cases of Strongyloides infection. In these patients, larvae were not found in the feces.

The diagnosis of psychoneurosis may not be warranted in the veteran with the syndrome described in this report.

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MEDICAL PROGRESS

CANCER

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A POSTWAR survey of practice and theory in relation to cancer problems shows little fundamental change in comparison with the prewar years, although in some fields there have been modifications and shifts in emphasis. This review can make no pretense of being complete, but it seems desirable to comment on certain aspects of the problem.

Carcinoma of the Mouth

There appears to be an increasingly accurate discrimination regarding the respective fields of radiation and surgery in the treatment of primary intraoral carcinoma.[1,2] The former division into separate camps, with exclusive use of radiation in some clinics and exclusive use of surgery for operable cases in others, has given place to a willingness to concede the value and merit of the other approach. This has come about through accurate critical analysis of the results achieved in cases of carefully defined location, extent and histology. Radical surgery is applicable primarily in small accessible tumors that are of a relatively low grade of malignancy. The more extensive high-grade lesions are better suited to radiation therapy. The results of this treatment have improved with the employment of greater dosage. There has also been clarification of the indications for neck dissection, as well as of the benefit that may be expected as a result of dissection.[3]

Carcinoma of the Larynx

Similar clarification is desirable in laryngeal carcinoma. Cutler[4] has presented an impressive series of cases treated by a modified Coutard method of radiation. Schall[5] and others have successfully employed laryngectomy in a large number of cases. It is probable that many of the patients treated by laryngectomy might have been cured by radiation. It is also possible that certain of the cases that proved to be refractory to radiation might have been successfully treated by laryngectomy. Analysis of the clinical and pathological characteristics that contribute to a successful outcome by one or another method of treatment should be carried out at every opportunity.

Mixed Salivary Tumors

In spite of the sustained interest of McFarland[6] in the mixed salivary tumors, their origin and possible relation to the development of carcinoma remain obscure. In general, these tumors are smaller when the patients first seek advice than they were several years ago. Earlier textbooks describe the characteristic tumor as the size of a walnut, or even an egg. In recent experience, such large tumors are distinctly unusual in this community. The apparent tendency to evolve toward benignancy with increased duration and size, noted by McFarland, may be explained by the fact that the larger tumors are operated on with more respect and more radically. The propensity to recur following simple excision has led to increasing employment of the Adson–Ott operation,[7] in which the entire gland superficial to the facial nerve is resected, including the tumor. The excellent anatomical studies of this region by McCormack et al.[8] should be reviewed by all surgeons who undertake to perform this operation.

Carcinoma of the Thyroid Gland

There is general agreement that thyroid carcinoma usually originates in a pre-existing pathologic condition of the gland, frequently in a solitary nontoxic nodule. In fact, the incidence of carcinoma in solitary nontoxic nodules may be as high as 24 per cent,[9] or even higher.[10] There is general acceptance of invasiveness and blood-vessel invasion as criteria of malignancy. The problem at once arises concerning how much further surgery may be necessary when the pathologist unexpectedly returns a report of carcinoma in an apparently innocent nodule that has been removed at operation.

The high incidence of carcinoma in these nodules argues that excision be abandoned. Wide resection of the involved area or complete excision of the lobe should be carried out. This procedure is probably sufficiently radical when there is no clinical evidence of malignancy and when there is no pathological evidence of invasion of the gland capsule. When malignancy is suspected or when there is evidence of invasion of the gland capsule at operation, it is essential to carry out block dissection of the affected side. This involves removal of the sternomastoid, sternohyoid, omohyoid and sternothyroid muscles, the internal jugular vein from the junction with the subclavian vein to the lower pole of the parotid gland and the lymphoid tissue and fat from the anterior border of the trapezius muscle to the midline.

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Thus, the operation is essentially a radical neck dissection except that the submaxillary area need not be included. The likelihood of lymph-node metastasis as the sole or earliest manifestation of spread is great, especially in the relatively low-grade papillary adenocarcinomas.

Lahey[11] has again emphasized the likelihood of the development of malignant changes in aberrant thyroid nodules. It must be recognized that some tumors of this sort may be metastases from undetected primary foci of disease in the thyroid gland itself.

The use of thiouracil in the treatment of hyperthyroidism involves some consideration of its possible relation to carcinogenesis in the gland. Bielschowsky[12] reported the development of cancer of the thyroid gland in experimental animals by the use of a carcinogen, 2-acetyl-amino-fluorene, in conjunction with allyl-thiourea. Neither compound alone was capable of producing thyroid carcinoma in control animals.

Carcinoma of the Breast

Foote and Stewart[13] have made a major contribution to the pathology of benign breast conditions and their relation to carcinoma. Haagensen and Stout[14] reported an exhaustive analysis of their experience with carcinoma of the breast, especially analyzing the prognostic significance of certain clinical manifestations of the disease. Their experience was closely paralleled by that of Wells[15] and, indeed, coincides with that of most other clinics where a considerable number of these patients are treated. Variations in the criteria of operability probably account for variations in results. The use of estrogens in the treatment of advanced carcinoma of the breast, especially in patients beyond the age of sixty, promises to be a valuable palliative procedure in some cases.[16, 17] It is too early to discover how long the regressions may be maintained. The use of testosterone has also brought about regressions in certain cases.[18]

Carcinoma of the Lung

Tremendous strides have been made in recent years in the technics of thoracic surgery, and significant series of radical operations for lung carcinoma are now recorded. Lindskog[19] called attention to the low operability rate for radical procedure and the advanced stage of disease presented by most patients when first seen. Mass screening by chest x-ray examination, which has successfully been carried out for tuberculosis, might be applied to a large group in an attempt to find cancer of the lung in a presymptomatic and favorable stage. Herbut and Clerf[20] have applied the Papanicolaou method of examination to sputums, with encouraging results.

Carcinoma of the Esophagus

In no field has the development of thoracic surgery led to such rapid progress as in the problem of carcinoma of the esophagus and of the cardiac end of the stomach. Sweet[21] has reported a brilliant series of esophageal resections, with a constantly diminishing mortality. It is discouraging to discover that lymph-node metastases are frequent, occurring early, and that attempts to include many of them in the resection are not successful. Even as a palliative procedure, however, the operation is highly successful. A similar approach and technic give excellent access to carcinomas at the cardiac end of the stomach, in which the results are also promising.[22]

Carcinoma of the Stomach

As in carcinoma of the lung, a discouraging picture applies to carcinoma of the stomach in the fact that operability rates for radical excision remain relatively low. Wangensteen[23] and his co-workers undertook screening by gastric analysis, followed by further investigation of the achlorhydric patients. In this fashion they found a significant number of patients with gastric polyps, which are often conceded to be precancerous. Various authors[24, 25] have extended the indications for radical surgery in most abdominal carcinomas to include a large group with fixation to adjacent organs and with metastases in the liver and spleen. Although these operations are a challenge to surgical skill and to the restorative and antishock efforts of the team, it is doubtful whether much good is accomplished, even as palliation.

Carcinoma of the Pancreas

The development of the Whipple[26] operation and its various modifications have made it possible to attack carcinomas of the pancreas,[27] duodenum and bile ducts[28] with greater assurance, lessened operative mortality and an increased likelihood of success. These advances are due not only to technical progress but also to improved understanding of maintenance of physiologic equilibrium.

Carcinoma of the Colon and Rectum

In recent years a revived employment of open resections in the colon has been made possible in part by improvements in technic and in part by the use of decompression as a safeguard, as well as by the use of chemotherapeutic agents, especially sulfathalidine and succinylsulfathiazole (Sulfasuxidine). The increased safety of open resections has led to a revival of procedures to preserve the anal sphincter and to avoid a permanent colostomy in dealing with growths that are low in the colon.[29–31] Some im-

petus has been given to this trend by the anatomical studies of the lymphatic drainage areas carried out by Dukes,[32] Grinnell,[33] Kay[34] and others. Their findings establish that downward lymphatic spread from rectal cancer is rare and only likely to occur when the upward-draining lymphatic vessels are blocked by cancer metastases. These conservative operations are technically difficult and probably not so sound as the more orthodox procedures from the point of view of a thorough operation. The likelihood of postoperative complications appears to be greater, and the prospect of adequate function of the preserved sphincter is problematical. In addition, whereas the procedures perhaps fulfill the requirement so far as lymph-node involvement is concerned, they appear to disregard the fact of venous involvement, which is increasingly recognized as significant.

An important study of carcinoma of the rectum on a state-wide basis has recently been presented by Ottenheimer,[35] who reports the experience in Connecticut. The value of such a survey cannot be overemphasized. It serves both to define the problem and to provide a base line against which progress can be measured. Although other states may plead the increased difficulties of such surveys in a heterogeneous population, the value of this approach to cancer of various regions is obvious. It is to be hoped that further studies on other groups will be carried out.

Carcinoma of the Cervix

The Papanicolaou[36] test for cancerous cells in the vaginal smears has been hailed with some enthusiasm as a method of screening patients to find carcinoma of the uterus in a presymptomatic stage. In the hands of competent interpreters of the slides it may achieve a high degree of accuracy. The method has been applied to other secretions, such as sputums, gastric washings and the contents of cysts. It may prove to be a useful adjunct to diagnostic procedures. It is probably too protracted and too dependent on expert interpretation for use as a routine screening procedure on a large completely asymptomatic group of patients.

Meigs[37] has continued his series of Wertheim operations in selected cases of carcinoma of the cervix. In the cervix, as in the larynx, radical surgery in selected cases yields excellent results. Radical radiation is also extremely effective, especially in early cases, whereas the selection of cases is not nearly so exacting. Here, as in the larynx, certain cases are refractory to radiation, and it is desirable to attempt more accurate identification of this refractory group. Taussig's[38] operation of iliac lymphadenectomy — a retroperitoneal dissection of the lymph-node areas — was designed to take care of lymph-node metastases following destruction of the primary cancer by radiation. Taussig found involved nodes in about 40 per cent of the patients submitted to the operation, in whom he obtained cures in about 25 per cent. Recently, Nathanson[39] accomplished the same objective by means of a retroperitoneal dissection through bilateral incisions in the groins.

Lymphoblastoma

The definitive classification of the lymphoblastomas was presented by Jackson and Parker.[40] Formerly, the terminology had been confusing, and it was often difficult to decide which group of tumors was under discussion in studies from various clinics. The work of Jackson and Parker, with its wealth of pathological material correlated with clinical progress, should lay the groundwork for appropriate therapeutic efforts.

Bone Tumors

In recent years, the clinician concerned with the diagnosis of bone disease has had to learn to recognize osteoid osteoma[41] and eosinophilic granuloma.[42] Although neither of these tumors is a true neoplasm, their occurrence and identification has probably added another difficulty to an already confusing problem. Fortunately, both lesions are benign and respond readily to appropriate surgical measures.

Carcinoma of the Prostate

Although Huggins[43] first reported his experiences in the treatment of carcinoma of the prostate by orchiectomy and estrogens several years ago, the literature still contains reports of successes, and there is some question regarding the duration of the remissions and the types of the disease likeliest to respond favorably. It is probable that several more years will elapse before final appraisal of this undoubtedly valuable adjunct of treatment.

Radiation Therapy

Holmes and Schulz[44] have published the results of million-volt x-ray therapy. They found less skin damage from the dose delivered to the tumor than with lower voltages. The results of treatment appear to be superior in carcinoma of the bladder,[45] cervix, lung and tonsil.

Miscellaneous

Pack and Ehrlich[46] published technics as well as a series of cases of radical amputations, including the shoulder girdle, hip joint and sacroiliac. These mutilating procedures are occasionally indicated in extensive malignant processes, and as the authors point out, they may be indicated for palliation in some cases.

The criteria of malignancy have already been referred to in the discussion of thyroid carcinoma. The clinician is too ready to accept as fact the diagnosis offered by the pathologist without recognizing that such a diagnosis is a conclusion and judgment based on an assembly of data. One is occasionally

confronted with tumors whose clinical behavior is at variance with their histologic character. It is for this reason that great interest centers on the work of Greene and Lund,[47] who succeeded in growing human malignant tumors in the anterior chamber of the guinea-pig eye. This capacity for growth is apparently not shared by benign tumors, and the procedure may prove of value in determining the nature of a tumor in which the histologic character is obscure or equivocal.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 33061

PRESENTATION OF CASE

First admission. A forty-three-year-old automobile dealer was admitted to the hospital because of chest pain.

On the previous day the patient had suddenly been seized with pain beneath the sternum and upper back, noted especially on deep breathing. The pain persisted, growing worse when he was lying down, and kept him awake for a time, although he felt better on the following day. Work intensified the pain, especially when he stooped. He visited a physician, who found no fever, hoarseness or pharyngeal congestion, but because of a white-cell count of 20,000 he was referred to the hospital.

The patient had had two gonorrheal infections, the second one occurring three years previously. Both had cleared with therapy. He smoked constantly and took small amounts of alcoholic drinks regularly.

Physical examination revealed that the heart was not enlarged and that the sounds were of good quality. Nothing else of note was found.

The pulse was 110, and the blood pressure 150 systolic, 90 diastolic.

Examination of the blood showed white-cell counts of 9000 and 12,500, with normal differential counts. The urine was normal. X-ray examination of the chest was negative. An electrocardiogram disclosed rather low QRS complexes in Leads 1, 2 and 3 but normal ST segments and T waves in all four leads. The patient was discharged two days after admission.

Second admission (two years later). The patient had had no further symptoms since the previous admission until he was again admitted for chest pain. About 1:00 a.m. on the day before admission the patient awoke with an aching substernal pain penetrating to the back and spreading to both shoulders and down both arms. He arose and stayed up the rest of the night. The pain lessened during the next day but persisted beneath the xiphoid and extended to the throat. Lying on the back eased it only slightly and sitting up or lying on either side made it worse.

Physical examination revealed a split aortic second sound along the left sternal border but no enlargement of the heart or other abnormalities. The temperature was 100°F.

Examination of the blood disclosed a white-cell count of 21,900, with 95 per cent neutrophils, with a shift to the left. The hemoglobin was 16.5 gm. The urine was normal except for a ++ test for albumin and 150 white cells per high-power field in the sediment. An x-ray film of the chest revealed a moderately enlarged heart with prominence in the region of the left ventricle. Fluoroscopically the pulsations were weak. The aorta was somewhat tortuous, without evidence of dilatation. The lung fields were clear except for a small area of increased density in the right base. A barium swallow showed a small hiatus hernia. An electrocardiogram revealed normal rhythm and a rate of 95. There was high origin of the T waves in Lead 1, with moderate late inversion, a flat T_2 and a diphasic T_3. The QRS complexes were low in the limb leads, and the precordial leads showed an absent upright R wave in Leads CF_3 and CF_4, with high origin of the ST intervals in Leads CF_4 and CF_5 and late inversion of the T waves.

By the second hospital day the pain had disappeared and did not recur even on deep inspiration. Examination of the blood showed a white-cell count of 13,200. A gastrointestinal series revealed redundancy of the duodenum between the first and second portions. An electrocardiogram four days after admission showed a slight change in the appearance of the ST intervals: ST_1 appeared more elevated, and T_2 was definitely inverted. ST_3 was more depressed, and in the precordial leads there was more elevation of the ST intervals and less late inversion. After two weeks the patient was transferred to a convalescent hospital, where he remained for three weeks.

Final admission (four months later). The patient returned to the hospital because of recurrent pain in the chest. Following discharge he had restricted his activity for a while and had then gone for short walks. He was able to climb three flights of stairs without difficulty, and during the third week he tried a short period of work at the office. That night, however, he had a severe attack of precordial pain radiating to both arms and to the back. He was seen by a physician, who observed a blood pressure of 150 systolic, 100 diastolic, and an apical gallop rhythm. The pain lasted for two days, and the patient remained in bed until a week before admission, when he was allowed to sit in a chair. He occasionally developed some swelling of the ankles while sitting up. At 4:00 a.m. on the day of admission he had another attack of substernal pain, without radiation, but exaggerated on deep breathing.

Physical examination showed the patient to be in moderate discomfort, with steady substernal pain. The heart was moderately enlarged. The pulse was 96, with multiple extrasystoles. Crackling rales were heard at the left base, and the neck veins were prominent. The blood pressure was 104 systolic, 74 diastolic.

Examination of the blood revealed a hemoglobin of 14.5 gm. and a white-cell count of 20,400, with 84 per cent neutrophils and a shift to young forms. The urine showed a + test for albumin, and the sediment contained 20 white cells per high-power field. An electrocardiogram showed normal rhythm at a rate of 100, interrupted by ventricular premature beats. The QRS complexes were low in the limb leads. The T waves were flat in Lead 1 and low but diphasic in Leads 2 and 3; the PR interval was 0.18 second. The precordial leads showed inverted QRS complexes in Leads CF_2 and CF_4, with upright T waves and a flat T wave in Lead CF_5.

Anticoagulant therapy with dicumarol was instituted, and the prothrombin time was maintained at an average of approximately 40 seconds, with a control of about 18 seconds. The patient showed improvement during the first ten days of hospitalization, but subsequent electrocardiograms revealed slightly higher voltage in the limb leads and more inverted T waves in Leads 1 and CF_5. On the morning of the twenty-first hospital day, as on previous mornings, he complained of a sensation of "fluttering" and of "water" rushing through the precordial region but no pain. On physical examination the rhythm was grossly irregular, characteristic of fibrillation, but this changed shortly to a normal sinus rhythm, with frequent extrasystoles every third to fifth beat. The rate was about 92. He was discharged on that day.

The patient continued to take dicumarol, with frequent checks of the prothrombin time, which maintained an average of 40 to 50 seconds. After several weeks of rest in bed he gradually resumed physical activity and even returned to his office part time, but found it increasingly difficult to adapt himself to the disease. He became depressed, began to drink liquor freely, and had mild anginal attacks for two weeks. He died suddenly about three months after discharge.

Differential Diagnosis

Dr. Edward F. Bland: We need spend little time in the discussion of the differential diagnosis, since it is obvious that the relatively new method of treatment employed in this case is the point of chief interest. Attention might be called, however, to the first episode of pain at the age of forty-three. The diagnosis in that attack from the clinical description is a little uncertain. The trouble was most probably of coronary origin; it could have been a pulmonary infarct. The pain was steady, and breathing caused discomfort. It is slightly unusual for the pain of a myocardial infarct to be sharply accentuated by breathing. That observation usually points to the lung, pleura or pericardium. There was no proof of a pulmonary infarct by x-ray examination or of a myocardial infarct on the electrocardiograms. The clinicians apparently did not consider this a serious illness, because the patient was permitted to return home the next day. The subsequent course supported their decision, because there was no further trouble for two years.

The second episode, at the age of forty-five, was clearly, I believe, a coronary occlusion. The character of the pain radiating down both arms and the characteristic findings in the electrocardiogram pointing to a myocardial infarct at the apex of the heart leave little doubt regarding the diagnosis. The fact that the blood pressure did not drop need not be considered because when patients are seen during the course of coronary thrombosis — if they are having pain and if vascular shock has not occurred — the pressure is likelier to be elevated than the reverse. Furthermore, there was some enlargement of the heart. The statement in the x-ray report of slight density at the right base raises the possibility of a complicating pulmonary infarct. I shall ask Dr. Schatzki about that later.

Dr. Richard Schatzki: There are no x-ray films.

Dr. Bland: We might proceed then to the third episode of pain, which was severe enough to cause the patient to come to the hospital. At that time he had signs of heart failure. The electrocardiogram showed changes from the previous record, but it must be remembered that he was probably taking digitalis, although it is not so stated in the record. I believe that this episode was also caused by myocardial infarction.

A fourth attack of severe pain, which occurred in the hospital, could have been due to a pulmonary or a myocardial infarct, most probably the latter. From this sequence of events I believe that there is no doubt that this man was suffering from severe coronary heart disease, with recurring episodes of myocardial infarction and possibly occasional pulmonary infarcts, and that he ultimately died abruptly in a manner characteristic of severe coronary disease.

Let us pass to the therapy, which introduces, I suspect, the real reason for bringing up this case — namely, the use of anticoagulants under these circumstances. During the past year there have been three reports in the literature concerning the use of anticoagulant therapy following acute myocardial infarction. The evidence is suggestive that such a procedure may be helpful in inhibiting complications. Statistics reported by Barker[1] indicate that following an acute myocardial infarct there is approximately a 35 per cent chance that patients within the first six weeks will have some form of thromboembolic complication, if one includes both peripheral thrombophlebitis and pulmonary infarcts, as well as thrombi in the heart and consequent peripheral emboli. Actually that figure seems too high to me. Nevertheless, the risk of such complications is considerable. In the face of this, anticoagulant therapy seems rational to prevent these thromboembolic complications. Furthermore, there has been at least one report mentioned by Barker[1]

suggesting that the use of anticoagulants in patients who are having recurrent episodes of coronary thrombosis inhibits to some extent the formation of further coronary thrombi. I should be less hopeful, perhaps, about preventing these recurring episodes by this form of therapy than of lessening the chances of complications. In this connection, a report last summer in the *Journal of the American Medical Association*[2] recorded a series of 110 cases of acute myocardial infarction; 60 of these patients were used as controls, and 50 were given anticoagulant therapy in the form of dicumarol. Of the control group 16 per cent developed clinically manifest peripheral emboli, and only 2 per cent of the treated group developed clinical embolism. That is a significant difference. Furthermore, the deaths in the treated group were much fewer than those in the untreated group. This problem obviously requires extensive study and observation, preferably by more than one clinic or one group. Therefore, the American Heart Association has embarked on a project to study a large number of cases in several clinics under a controlled program so that each investigator will more or less follow the same scheme. The present arrangement is to treat alternate cases of acute myocardial infarction with anticoagulant therapy. Such a program is now in progress in this hospital, as well as in several large hospitals elsewhere in this country. The answer remains to be seen.

What are the possible disadvantages of this therapy? A large mural thrombus might serve as a blow-out patch to prevent actual rupture of the heart. If the stoutness or extent of the thrombus is lessened, more cases of rupture of the heart may theoretically be expected. Perhaps Dr. Mallory will express an opinion on that score. Furthermore, I have discussed with the surgeons what their reaction would be to a patient in whom, in spite of dicumarol therapy, a femoral artery suddenly occluded. Would they hesitate to do an embolectomy? They have not yet encountered this situation, but operation would not be contraindicated in spite of a prothrombin time between 35 and 50 seconds, which is the effective therapeutic level. There is one further probable indication for anticoagulant therapy in acute myocardial infarction: irritability of the heart with paroxysms of auricular fibrillation, which, as is well known, is prone to result in thrombosis in the auricle and embolism peripherally.

In conclusion, it seems that this case afforded an ideal situation for this new and special form of therapy. We believe that it is reasonably safe. Before Dr. Mallory tells us the post-mortem findings, I think that the clinical record should be clear. It is implied but not definitely stated that the patient was kept on dicumarol up to the time of death.

Dr. James H. Currens: That is correct.

Dr. Bland: We therefore have an opportunity in this case to see what thrombotic phenomena were present after a patient had been on dicumarol for three months. I know of one patient kept on anticoagulant therapy for a period of six months without untoward effects.

Dr. James H. Townsend: Would you predict where the various infarcts were?

Dr. Bland: That would lead us into a somewhat detailed discussion in this case.

Dr. Townsend: Which one occurred in which of these admissions?

Dr. Bland: In the second episode the electrocardiogram, as I have previously stated, was characteristic of an infarct in the region of the apex. The subsequent changes in the electrocardiogram with the third episode were rather noncommittal, suggesting further injury in the same region, or perhaps the electrocardiogram was modified either by the use of digitalis or by an infarct at the base. I should prefer not to go into great detail on that point. I think that the major infarct was at the cardiac apex. I should not be surprised if there were multiple infarcts in the heart, some large and some small, or if autopsy showed some old scars in the lung, possibly healed pulmonary infarcts.

Dr. Benjamin Castleman: What do you think was the cause of death?

Dr. Bland: The patient died suddenly, as many patients with severe coronary disease do. I wondered perhaps if the heart had ruptured at the end. If it did, one must presuppose a fresh myocardial infarct, because healed infarcts do not rupture. The only clue was the two-week period of angina pectoris near the end, which may have represented further softening in the myocardium. In most people who die suddenly with coronary disease, however, we find simply marked coronary narrowing with areas of old infarction and occasionally a tiny fresh clot in one of the chronically obstructed coronaries, but usually not enough time elapses for microscopical or gross infarction to become evident. Many patients in the presence of marked coronary disease succumb suddenly, and we are unable to determine any specific additional cause of death at that particular moment. Perhaps it is cardiac standstill or ventricular fibrillation. Was quinidine given to this patient?

Dr. Currens: No.

Dr. Bland: Was digitalis given?

Dr. Currens: I believe that it was.

Dr. Bland: I shall be surprised if Dr. Mallory says that the patient had a ruptured heart. I suspect that no specific cause for the final exitus, other than extensive coronary disease, was found.

Dr. Castleman: In the new project, how long is a patient kept on anticoagulant therapy?

Dr. Bland: Six weeks. This project has just started. I do not know the laboratory details. Only one patient has been treated, and he died on the

third day; he had a massive myocardial infarct. We have not yet had enough experience with this new project to make definite statements.

Clinical Diagnosis

Coronary thrombosis, recurrent, with myocardial infarction.

Dr. Bland's Diagnoses

Coronary heart disease.
Myocardial infarcts.

Anatomical Diagnoses

Coronary sclerosis, severe.
Myocardial infarcts, anterior, old, and posterior, recent.
Pulmonary congestion and edema.
Horseshoe kidney.

Pathological Discussion

Dr. Tracy B. Mallory: Post-mortem examination showed a considerably hypertrophied heart, which weighed 550 gm. All the branches of the left coronary artery were markedly sclerotic and partially calcified with fibrous narrowing. There were, however, minute pin-point lumens suggesting that thrombi had been recanalized. No acute change was found in the coronary arteries to explain why this man died at the particular moment that he did. The left ventricle showed two definitely separable areas of infarction. One on the anterior surface, well toward the apex, was very old and fibrous. The second one, which was found on the posterior surface and slightly toward the base, was also of considerable duration — some weeks at least. It was probably responsible for the third episode. The endocardium over both infarcts was thickened and sclerotic, but there were no fresh thrombi. The lungs showed marked congestion, indicating that there had been sudden left ventricular failure, which must have lasted for a few minutes before death.

The only other finding was an anatomical curiosity, a horseshoe kidney. which I am sure had no significance.

On microscopic examination the liver showed a rather extensive fatty vacuolization — more than could be accounted for by heart failure — but could be explained by the alcohol to which the patient turned for consolation during the last few months of life. It had not progressed far enough, however, to produce any degree of liver insufficiency.

Dr. Currens: One or two features of the clinical course were interesting. In a period of four months the patient had four episodes of pain entirely consistent with the diagnosis of coronary thrombosis. Because of these recurrent attacks, it was decided to place him on dicumarol therapy. He was certainly a suitable patient to follow for a time. All four attacks of pain appeared at night, awaking him from a sound sleep. The blood pressure was found to be quite low, particularly in the morning, the diastolic pressure being 50 and the systolic 80 to 90. At the time of the pain, however, the arterial bed was able to constrict and produce moderate hypertension.

So far as dicumarol therapy is concerned, it was easy to carry him and maintain a prothrombin level between 20 and 40 per cent with 15 mg. of the drug after the initial dicumarolization. The dosage varies tremendously from patient to patient, and the individual daily dosage must be established if one decides to carry it over that length of time. The fact that there was no evidence of recent infarction or thrombosis may be significant.

Dr. Bland: It is also significant that the lungs were clear so far as pulmonary emboli were concerned.

Were the peripheral vessels examined?

Dr. Mallory: They were not examined, since we found no infarction in the lung.

Whenever a new drug is introduced the pathologist naturally looks for manifestations of toxicity. The only evidence of dicumarol toxicity described to date is extensive hemorrhage with uncontrolled dosage.[3] Patients have died with subarachnoid, gastrointestinal and renal hemorrhages. There was no manifestation in this case that could have been considered evidence of toxicity.

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CASE 33062

Presentation of Case

A sixty-seven-year-old housewife entered the hospital because of recurrent abdominal distention and pain.

Six years before admission the patient had had a single attack of abdominal pain, without diarrhea, for which no explanation was found. Five years later an attack of distention, with fever, constipation and abdominal distress, occurred. A plain film of the abdomen showed a large amount of gas and fecal matter distending the colon. The barium enema reached nearly to the splenic flexure. The whole descending colon was distended with feces, and the patient was unable to retain the enema. There was considerable spasm in the sigmoid, and a few diverticulums were seen. With colonic irrigation and mineral oil by mouth the symptoms ceased, only to recur again in ten days. Examination of the abdomen was negative except for distention, which cleared after a day or so. Eleven months before admission, the patient was having colicky, non-

localized, midabdominal pains, but the bowels moved freely. A questionable mass was palpated in the left lower quadrant. A month later the bowels were sluggish, and there was some distention but no pain. Seven months before admission an occasional, mild abdominal pain occurred. The abdomen was soft. A month before admission the bowel movements were loose, and there had been increasing anorexia and a weight loss of 10 to 15 pounds. Three weeks before admission barium-enema study was negative except for marked dilatation of the cecum and the ascending and the transverse colon. The distention became more persistent, and during the week before admission frequent enemas were required for relief, although the bowel movements were spontaneous and normal. The patient vomited small amounts once or twice daily. Four days before admission a colonic irrigation gave considerable temporary relief.

Some years before the present illness an appendectomy had been followed by a phlebitis in the left leg. There had been attacks of mild cystitis ten, two and one years before admission, each lasting from a week to a day. Ten years before admission the pelvis had been fractured in an automobile accident.

Physical examination disclosed an obese patient who nevertheless showed signs of weight loss. The abdomen was distended, soft and nontender. Peristalsis was increased. No mass was felt. There were external hemorrhoids. Rectal examination was negative.

The temperature was 98.2°F., the pulse 88, and the respirations 20. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 14.2 gm. and a white-cell count of 9700, with 82 per cent neutrophils. The urine was normal. No ova, parasites or red cells were found in the stools on repeated examination. The stools were guaiac negative. A barium enema revealed an area of rather marked narrowing in the middle and upper sigmoid over a distance of approximately 12 cm. The lumen was irregular, and in the midportion there was an uneven area that could have represented a pocket extending beyond the bowel lumen. There were a few diverticulums in the distal sigmoid, but none in the region of the narrowing. The margins of the latter were not shelved. Barium passed beyond the obstruction showed considerable fecal material in the dilated colon. The small bowel was also dilated. Fluoroscopically there was thought to be a shadow behind the heart, possibly a hernia, but this did not contain colon.

On the second hospital day, proctoscopic examination was negative up to 15 cm. above the anus. The patient's condition continued unchanged for nine days, when a cecostomy and a prophylactic bilateral femoral-vein ligation were performed. The postoperative course was satisfactory. The colon was drained by a Miller–Abbott tube inserted through the cecostomy. The small-bowel distention gradually decreased but did not disappear. The urinary output, which was low for two days, subsequently increased. The serum protein had dropped to 3.6 gm. per 100 cc. by the fifth postoperative day. The white-cell count reached a maximum of 16,000 on one occasion; a transfusion with 500 cc. of blood was given at the time of operation, and again on the fifth postoperative day. On the twenty-third hospital day a second operation was performed.

Differential Diagnosis

Dr. Francis D. Moore: This woman in the seventh decade of life, after six years of vague abdominal rumbling, which presaged further trouble, developed abdominal symptoms in a gradual crescendo that reached a maximum at the time of admission, when the previous, rather vague and intermittent symptomatology yielded to symptoms of obstruction with anorexia and weight loss. The significant items of that six-year history are the duration and the finding, a year before admission, of diverticulosis with spasm in the sigmoid, justifying a diagnosis of diverticulitis. This bout of difficulty had evidently subsided spontaneously, only to recur on various occasions prior to admission, the most recent episode taking the form of an intensified version of the previous ones.

The past history does not cast a great deal of light on the present symptoms except that, since the appendix had been removed, we presumably need not worry about that as a source of the present trouble.

On physical examination, the patient was noted to be obese, which as I shall point out later is probably significant. Examination of the abdomen showed low-grade, large-bowel obstruction. The patient was not systemically ill and had little evidence on physical or laboratory examination of invasive infection. The negative guaiac test was of course of great interest and probably significant, although it would be nice to know whether multiple tests were carried out. The x-ray findings, needless to say, are of the greatest importance.

X-ray study revealed narrowing, with neighboring diverticulosis. We need not waste time on the well known fact that the diverticulums involved in acute diverticulitis often do not show in the x-ray film, owing to the fact that they are filled with purulent material, to edema of the mucosa or to fecal material, or to a combination of the three. The significant facts are that the margins of the defect were not shelved and that some obstruction was produced. Dilatation of the small bowel simply indicates that the ileocecal valve was not competent. The negative proctoscopic examination is of little help one way or another, since the patient's lesion was well above 15 cm. from the anus. The lack of

blood on proctoscopy, however, corroborates the negative guaiac test.

The initial operation performed — namely, a cecostomy and prophylactic bilateral femoral-vein ligation — is of some interest from a technical point of view, because it might have been predicted that a transverse colostomy would be a more satisfactory initial procedure in this particular patient. I imagine that prophylactic bilateral femoral-vein ligation was carried out not only because of the patient's age and the disease but also because of the previous phlebitis. After this operation the colon was drained by a Miller–Abbott tube inserted through the cecostomy, an ingenious method of large-bowel lavage worked out by Dr. J. B. Millet.[1] Again, I should like to know what disease the surgeons thought they were dealing with because, even with Miller–Abbott lavage of the large bowel through a cecostomy, I should not consider the bowel adequately prepared for resection of an inflammatory process. After this operation the urinary output was low for two days but subsequently increased, suggesting that the physiologic disturbance incident to operation was greater than had been expected. At the end of that time the serum protein was 3.6 gm. per 100 cc., and one wonders if this was an accurate determination or if the patient had possibly been overhydrated in an attempt to restore the renal function. On the twenty-third hospital day, after a transfusion, a second and presumably definitive operation was performed.

The differential diagnosis lies between carcinoma of the sigmoid and diverticulitis. There are a few other extremely rare conditions to be considered, such as endometriosis, invasion of the large bowel by tumor of a neighboring viscus and some of the rarer bowel tumors.

Because of the fact that the patient had had symptoms for six years, as well as a known diverticulosis and typical diverticulitis with spasm a year previously, and because of the negative guaiac test and the fact that no shelf was visible in the x-ray film, I take the point of view that the patient had diverticulitis, with spasm and obstruction, and a small area of localized perforation represented by the pocket of barium outside the lumen. She obviously had little systemic reaction to this perforation, which was probably chronic and caused no elevation of the white-cell count or temperature.

From time to time someone gets up enough curiosity concerning the subject of diverticulitis to look up a series of cases of this disease. Reviews by Smithwick,[2] in 1942, and Morton,[3] in 1946, are examples of such clinical investigation. It might be worth while to review some of the figures in one of those articles and to determine whether our analysis of this case agrees with the figures in the article. According to Morton, diverticulosis is found in approximately 7 per cent of all post-mortem examinations. This is merely another way of saying that one should not be too much influenced by the diverticulums found in the x-ray picture.

In 200 cases of diverticulitis, 111 patients entered the hospital with diverticulitis and spasm, meaning that local narrowing in the sigmoid was an accompaniment of the systemic manifestations. The combination was noted in obese patients about four times as often as it was in thin patients and was equally distributed between men and women. Essentially all the patients were over forty years of age, and 94 per cent had pain as the outstanding symptom. About a third of these patients had distention, and it is of interest that in Morton's series 24 per cent gave a distinct history of having passed bloody stools and that in 32 per cent the benzidine test was positive for occult blood. This evidence shows that blood in the stools does not rule out diverticulitis; it is obviously important to mention, however, that with blood in the stools one must be suspicious of the diagnosis of diverticulitis and treat such patients with the presumption that carcinoma is present. In this particular case, however, since the guaiac test was negative and proctoscopic examination revealed no blood, the diagnosis inclines toward diverticulitis.

In Morton's series, 85 patients, or slightly less than 50 per cent, had various complications of diverticulitis. These complications were equally divided between perforation and obstruction; it is worthy of note, however, that perforation carried a 30 per cent mortality. It is also of the greatest importance to observe that 17 of these patients had carcinoma. The neoplasms were in the sigmoid in 12 cases and elsewhere in the colon in 5. This may be stated otherwise by pointing out that 10 per cent of patients who have diverticulitis with complications also have carcinoma of the colon. The significance of this consideration in evaluating this particular patient is obvious.

It is also worthy of note that 25 per cent of the obstructed patients also had a small abscess, which would apply to this patient, and that 50 per cent of the obstructed cases were completely obstructed. The patient in the case under discussion was not completely obstructed.

Thus, when we try to determine how this patient fits into the broad picture of diverticulitis, we see that in many ways she is quite typical of patients with the disease.

That brings us to the final point of the difference between the surgical diagnosis and the surgical strategy in handling a case. My diagnosis in this case is diverticulitis, with partial large-bowel obstruction and a small localized perforation producing an abscess.

In dealing with this patient, however, one must consider the lesion to be carcinoma until it is proved otherwise. By this I mean that, even when the

pathologist has the specimen on the table, he may not be able to tell whether or not a cancer is present, and the operation carried out must be radical enough to satisfy the requirements of cancer surgery. In view of the fact that considerable inflammatory process may be present, the bowel should be prepared in such a way that a safe resection can be done, if the lesion is diverticulitis — that is, by a transverse colostomy that comes as close to defunctioning the colon as is possible. It is my feeling that in this particular case another, possibly less satisfactory, maneuver was carried out, although it is only fair to say that on admission the patient may have had such a dilated colon that a satisfactory transverse colostomy would have been difficult or dangerous of accomplishment. In any event, after a suitable period of defunctioning of the distal end with an attempt to produce a surgically satisfactory and bacteriologically clean if not sterile bowel, an adequate radical resection of the area should be carried out with a diagnosis of diverticulitis but with a strong suspicion of carcinoma.

Clinical Diagnoses

Diverticulitis.
Carcinoma of sigmoid.

Dr. Moore's Diagnosis

Diverticulitis, possibly with superimposed carcinoma.

Anatomical Diagnosis

Diverticulitis, acute and chronic.

Pathological Discussion

Dr. Tracy B. Mallory: The specimen received in the laboratory was a segment of sigmoid measuring 25 cm. in length. The middle third was markedly indurated and narrowed and felt quite firm. Its serosa was covered with fibrin, the bowel wall was thickened to 6 mm., and the mucosa was thrown into pseudopolypoid folds. Numerous diverticulums were present in both the constricted portion and the proximal sigmoid above it. As Dr. Moore prophesied, it would have been impossible to exclude carcinoma on gross examination, but many microscopic sections showed only acute and chronic inflammation.

Dr. Arthur W. Allen: Dr. Moore has summed up this situation admirably. There was no question about the diagnosis of diverticulitis in this case. We were, however, confronted with problems that were perhaps not made entirely clear in the record. One was that, in spite of all our efforts, this woman maintained a serum protein level of about half the normal. We believed that she was much too distended at the time she came in for a transverse colostomy, which would have been the operation of choice. Also, she had dilated loops of small bowel, which might have indicated an incompetent ileocecal valve but were later proved to have been due to partial obstruction of the small intestine caused by adhesions to the inflammatory mass.

A cecostomy was done as a temporary measure. We had expected to do a transverse colostomy later after the decompression had partly subsided. Millet's method of deflating the colon with the Miller–Abbott tube was quite effective, but the patient still seemed to have dilated loops of small intestine. This caused us to attack the problem of relieving her of the secondary small-bowel obstruction. When the area was exposed, it was evident that she could not have improved had not the loop of small bowel attached to the inflammatory lesion been freed. This was easily accomplished, and it was not necessary to resect any small bowel. Instead of stopping at this point and hoping that the areas of small intestine would not become reobstructed, we elected to remove the disease in the sigmoid at the same time. A number of factors were involved in this decision.

We were dealing with a patient who, first of all, refused to have any surgery done. After five days, she agreed to let us proceed. When we told her that she would need three operative procedures before she was well, — namely, transverse colostomy, removal of the lesion at some later date and, finally, closure of the transverse colostomy, — she simply refused. A cecostomy was done, in the hope that possibly we might avoid a three-stage procedure and make it a two-stage operation.

At the second operation, after the small bowel had been freed, the sigmoid was carefully examined and felt not like diverticulitis alone but definitely like carcinoma. This influenced us somewhat in proceeding with a resection of the sigmoid at that time. We have seen carcinoma and diverticulitis associated in several cases and were swayed by this in removing this segment of the sigmoid. It proved however, that diverticulitis with a phlegmonous mesentery of the bowel was the true situation and that no cancer was present.

Dr. Moore: Dr. Allen's comments have filled out the picture in a fashion that would be difficult to put in the case protocol. Excessive distention certainly made an initial transverse colostomy impossible, and the continuing small-bowel obstruction forced the issue before further colonic preparation could be carried out.

My comments about the methods of preparation of the bowel were intended merely to bring out the point that adequate preparation of the segment to be resected is of the greatest importance if one is dealing with diverticulitis alone. One or two near disasters that we have had on the surgical service in the last two years, which resulted from resection

with inadequately prepared bowel, merely point out the significance of these considerations in diverticulitis.

The real difficulty, however, from a practical point of view, is nicely demonstrated by this patient and therefore is possibly worth an additional word. The problem can be stated as follows: if one is dealing with carcinoma, a resection after a week or two of preparation even by cecostomy alone, with or without the Millet device, is perfectly satisfactory, and in dealing with diverticulitis a total defunctioning transverse colostomy, with a rest of several months, is ideal. Yet from Morton's figures and those of others we find that diverticulitis and carcinoma coexist so frequently that the surgeon is often taking on himself an inordinate risk by letting the patient with what is considered to be diverticulitis rest at home for four to six months before resection is done.

Because of this fundamental problem and the difficulty of ruling carcinoma in or out we are often forced to a sort of compromise that in the occasional case of diverticulitis alone produces undesirable results. I recall well a patient in whom this differential choice existed and in whom I carried out a combined abdominoperineal resection with extensive pelvic dissection and, of course, a permanent colostomy, only to find that there was nothing but diverticulitis in the specimen.

I think that we should therefore give all the encouragement we can to those who are working on more adequate methods of diagnosing the presence of carcinoma.

DR. MALLORY: The postoperative complications that were feared developed in this patient. Gangrene of the bowel occurred on either side of the suture lines, followed by perforation and general peritonitis. There was a terminal bronchopneumonia.

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FOLIC ACID

The term "folic acid," originally used for a substance in spinach required for the growth of *Streptococcus lactis R*, is now applied to a group of substances found in yeast, liver, green leaves, cereals and other foods that are considered to be members of the vitamin B complex. The group includes vitamin B_c, required for the prevention of nutritional anemia in chicks, vitamin M, necessary for the prevention of nutritional cytopenia and a sprue-like syndrome in monkeys, and factors needed to prevent nutritional anemia in rats treated with sulfonamides to inhibit vitamin synthesis by intestinal bacteria. Also included are factors promoting the growth of *Lactobacillus casei* and *Str. lactis R.* The *L. casei* factor, also effective in the treatment of the animal nutritional deficiency syndromes mentioned above, has been isolated from liver and synthesized. It is a compound of a pteridine, related to the yellow color in butterfly wings, para-amino benzoic acid, a well known antagonist of sulfonamides, and glutamic acid, an amino acid, and has been named pteroylglutamic acid. Conjugates of this substance with two or six additional glutamic acid groups have also been isolated.

The interest to the medical profession in this group of substances lies in the ability of some of them to produce remissions in several nutritional macrocytic anemias, including pernicious anemia, and especially in the relation between pteroylglutamic acid and its conjugates and the principle in liver effective in Addisonian pernicious anemia.

The amount of solids in purified liver extracts is far less than the amount of folic acid required to give comparable hematologic effects, and the folic acid content of such liver extracts is negligible. In contrast to liver extract, folic acid is equally effective orally and by injection. It is thus clear that folic acid is not the principle in liver extract effective in pernicious anemia, nor is it the extrinsic (food) factor or the intrinsic (gastric) factor described by Castle. Folic acid does not restore the secretory activity of the stomach in pernicious anemia, at least so far as hydrochloric acid is concerned.

Liver principle is thought to produce folic acid, possibly by aiding enzymes known as conjugates in releasing free folic acid from the conjugated forms in which it appears in foods.[1] Folic acid, in turn, may act as an enzyme in the production of 5-methyluracil (thymine), a component of nucleic acid, which is also effective in pernicious anemia and related states but only in doses over a thousand times as great as that of folic acid.[2]

Nutritional macrocytic anemias that respond to injections of purified liver extract are thought to arise because of deficient intake of extrinsic factor, defective secretion of intrinsic factor or defective absorption of these substances or products of their interaction. Combinations of these mechanisms frequently exist. As was first shown by Spies and his associates,[3] folic acid acts approximately as well on the blood and bone marrow in these cases as purified liver extract. This group of anemias includes Addisonian pernicious anemia, megaloblastic anemia of

infancy and some cases of nutritional macrocytic anemia occurring with poor diets alone or in association with sprue, pellagra, chronic alcoholism, carcinoma of the stomach or pregnancy. In sprue it has been claimed that the stools improve and that the intestinal motility, atrophied mucous membranes and glucose-tolerance tests return to normal.

Purified liver extracts in the usual doses effective in Addisonian pernicious anemia do not relieve the anemia due to a deficiency of Wills's factor.[4] The anemia can, however, be corrected promptly by crude liver preparations. Such cases have been noted in association with defective diets, either alone or accompanying pregnancy or steatorrhea. Only three such cases have been treated with folic acid.[5] The response was partial, and further improvement followed crude-liver therapy.

The effective dose of folic acid is 5 to 20 mg. daily by mouth or by injection, 10 mg. daily being sufficient in most cases to produce remissions comparable to those obtained with purified liver extracts. Daily dosage seems advisable, since patients treated in this way may show maintenance of normal blood counts, whereas results are less satisfactory if folic acid is given in large doses every one or two weeks. This is not surprising in view of the fact that one third to one half of a 10-mg. dose of folic acid may be lost in the urine within twenty-four hours. No toxic effects have been noted with single doses as large as 400 mg.

Folic acid as a practical therapeutic agent does not, however, directly provide "new hope for anemics." Thus, there is no anemia that folic acid relieves that is not also relieved by liver extract. Crude liver extracts have produced complete remissions in cases due to a deficiency of Wills's factor after failure of folic acid to do so. Liver extracts are effective in the prevention and arrest of combined system disease, whereas there is growing evidence that neurologic disturbances in pernicious anemia may remain unaltered or even progress, sometimes in a rapid and dramatic fashion, under folic acid therapy, even when the red-cell count is maintained at a normal level.[6]

Two features of folic acid have been claimed as therapeutically useful. In the first place, it is suggested that oral therapy would remove the necessity for repeated injections. This, however, appears to be a disadvantage in pernicious anemia, since neglect of therapy occurs too frequently when patients treat themselves with oral medicines. In any case the possibility of neurologic complications outweighs any advantage that the oral route of treatment may have. Good health is usually maintained in pernicious anemia with an injection of 1 or 2 cc. of purified liver extract as seldom as every two or four weeks. Secondly, folic acid has been recommended for cases allergic to liver extracts. Dr. C. S. Davidson,[7] however, has recently shown that in a series of fourteen cases sensitive to pork-liver extract given parenterally all cases reacted favorably to beef-liver extract in spite of skin tests in some cases showing apparent sensitivity to the latter. These findings, together with the arguments mentioned above, make the use of folic acid in these cases unnecessary and undesirable.

Like liver extract, folic acid has failed to produce remissions in refractory and aplastic anemias, leukemias, myelophthisic anemias and iron-deficiency anemias, as well as in neutropenias occurring spontaneously or those due to sulfonamides, thiouracil or influenza. The possible beneficial effect of folic acid on the neutropenias due to exposure to radium and x-rays should be readily subject to analysis by animal experiment.

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TIME OUT

Even physicians need vacations whether they know it or not. One grows older insensibly; our confreres recognize this aging in us while we ourselves frequently do not. So likewise our professional duties pall, be it ever so gradually: our patients' little aches and pains, so real to them, irritate us and we are prone to brush them aside as irrelevant

and unimportant. We lose interest in our work and, perhaps, become irritable to others, and that very irritability galls us and makes us still more irritable. We develop aches and pains of no great moment and our doctor tells us that they are due to this or that organic defect — which, incidentally, we have had for the past ten years. This train of events increases in geometric proportion until something snaps, and even we ourselves recognize that we must cut the traces and be off, come hell or high water.

There are some physicians who, in actuality, do not need a vacation in the true sense of the word. These fortunate persons can keep themselves in fine fettle both mentally and physically by taking a long week end in the country now and then as the spirit moves them. They are to be envied. There are others who "knit up the ravelled sleave of care" by hurling themselves into the noisome turmoil of some large city. The great Nissl is said to have taken his time off by packing a small suitcase half full of cigars, covering them with a piece of cardboard and filling the remaining space with cigars. He then traveled by train — to nowhere in particular — until the intervening cardboard was reached. Then he retraced his steps. In other words, there are all sorts of vacations.

Where does the physician's physician fit into this picture? As a rule his problems are three: Is there anything really wrong? What is it? What should be done about it? Not infrequently the first question is the most difficult of all. There is both conscious and unconscious malingering. There is both conscious and unconscious rationalization of one's signs and symptoms. There is the unconscious tendency of the physician-patient to put two and two together and make five, just as there is, at times, a cheerful effort to put five and five together and garner one. The physician is notoriously a difficult patient. What knowledge he has, be it great or small, is liable to become distorted. He usually cannot evaluate his symptoms in an objective and dispassionate manner. Indeed, it is the rare physician who can sit back and say simply and without emotion: "Behold, I have this symptom. What shall I do about it?"

If this editorial seems to wander from the subject, it is because physicians, unless confronted by a concrete problem, are prone to do just that. The thesis is simply this: some men are ill and need meticulous care and protection, whereas others with symptoms no less severe are simply worn out mentally and physically and in grievous need of a vacation. It is then the attending physician's problem to size the situation up — to be sure that there is nothing really wrong, to take such measures as are necessary to prove that this is the case and then to insist that his patient take a vacation, one to his own liking and, above all, *sine die*. To place a sharp limit on the duration of a tired man's vacation automatically nullifies its beneficial effect.

It takes a brave and sagacious man to say to a fellow physician with marked symptoms: "Do you really want to take that trip? Then do."

MISCELLANY

NOTES

The appointment of three new professors at the Harvard Medical School has been recently announced. Dr. Robert E. Gross has been made William E. Ladd Professor of Child Surgery and head of the Department of Surgery at the Children's Hospital. Dr. William T. Green becomes clinical professor of orthopedic surgery and director of orthopedic surgery at the Children's Hospital. Dr. Joseph S. Barr becomes clinical professor of orthopedic surgery and director of orthopedic surgery at the Massachusetts General Hospital.

The following Massachusetts physicians were recently appointed fellows in the American College of Surgeons: Ronald W. Adams, Boston; Felicia A. Banas, Boston; James B. Blodgett, Boston; Francis M. Burke, Natick; Bradford Cannon, Boston; George D. Dalton, Quincy; Lawrence R. Dame, Greenfield; John F. Flynn, Pittsfield; George R. Gagliardi, Framingham; Ilia Galleani, Boston; Francis M. Ingersoll, Boston; Aurel G. Lavoie, Springfield; Samuel Levine, Lynn; Saul M. Marcus, Boston; Carroll C. Miller, Boston; Daniel L. Mooney, Fall River; Francis D. Moore, Brookline; Daniel J. Mullane, Brookline; Philip E. Mullane, Lowell; John A. Reidy, Boston; Arnold L. Segel, Boston; Clarke Staples, Malden; Joseph M. Stowell, Boston; and Charles L. Sullivan, Brookline.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Radio in Health Education. Prepared under the auspices of the New York Academy of Medicine. 8°, cloth, 120 pp. New York: Columbia University Press, 1945. $1.60.

This monograph is the first in a new series, entitled *Frontiers in Public Health Education*, and is intended for the use of health educators, social workers, radio personnel, health organizations and all others concerned with public health. The first part of the text is a critical analysis of radio broadcasting made under the auspices of the New York Academy of Medicine. The second part consists of papers presented at a public-health conference held in December, 1943, at which the various aspects of the radio program were discussed. An appendix gives a response analysis of a series of talks, entitled "Highways to Health," given over the air during the period from June 9, 1935, to November, 1939. A total of two hundred and twelve auditions were given on twenty-six different subjects. The number of talks on each

subject varied from thirty-nine on the problems in the care of children to two on varicose veins, goiter and other subjects. The average response was one hundred and ninety-four, and two tables show the responses higher and lower than the average. The highest response (nine hundred and twenty) was to a talk on the skin troubles of the young, and the lowest (two) was on the care of the skin in summer. It is interesting that the second highest response (nine hundred) was on arthritis. The radio is an instrumentality of communication with enormous potentialities, and the material presented in this monograph comprises a basic and critical evaluation of objectives and technics in radio health education. This monograph should be in all medical libraries and should prove valuable to all persons interested in public health.

The Diagnosis of Nervous Diseases. By Sir James Purves-Stewart, K.C.M.G., C.B., Knight of St. John of Jerusalem, M.D. (Edin.), F.R.C.P., consulting physician to Westminster Hospital, West End Hospital for Nervous Diseases and Royal National Orthopaedic Hospital. Ninth edition. 8°, cloth, 880 pp., with 358 illustrations. Baltimore: The Williams and Wilkins Company, 1945. $11.00.

This standard work, whose first edition was published in 1906, has been consistently revised throughout all its editions. The work has been rewritten so far as possible amid the strains of World War II. The author, while traveling from the United States to England in 1943, lost all his manuscripts and notes by enemy action and therefore had practically to rewrite the whole book on the basis of previous editions and material available in London.

Pediatric X-Ray Diagnosis: A textbook for students and practitioners of pediatrics, surgery and radiology. By John Caffey, M.D., associate professor of pediatrics, College of Physicians and Surgeons, Columbia University, associate pediatrician and roentgenologist, Babies Hospital and Vanderbilt Clinic, New York City, and consulting pediatrician, Grasslands Hospital, Westchester County, New York, and St. John's Hospital, Yonkers, New York. 4°, cloth, 838 pp., with 710 illustrations. Chicago: The Year Book Publishers, Incorporated, 1945. $12.50.

This is the first complete book on roentgenologic diagnosis in pediatrics published in English since that of Thomas Morgan Rotch, of Boston, on the diagnosis of diseases in early life by the roentgen method, issued in 1910. The author has based his work on the roentgenologic conferences held semimonthly at the Babies Hospital, New York City, during the last twenty years. The purpose of the work is to describe the shadows cast by normal and morbid tissues and the clinical appraisal of roentgenologic findings in pediatric diagnosis. Physics, technic and therapy have been omitted intentionally. To each topic is appended a short list of references to the literature. The book is well printed, with a good type, on coated paper. The illustrations are clear, and the roentgenograms clearly defined. This book should prove valuable in all medical-reference collections.

Surgical Treatment of the Motor-Skeletal System. Supervising editor: Frederic W. Bancroft, M.D., associate clinical professor of surgery, Columbia University, attending surgeon, New York City and Beth David hospitals, consulting surgeon, Veterans Administration, Lincoln and Harlem hospitals, New York, and Kings Park State Hospital, Kings Park, New York. Associate editor: Clay R. Murray, M.D., professor of orthopedic surgery, College of Physicians and Surgeons, Columbia University, attending surgeon and chief of the Fracture Service, Presbyterian Hospital and Vanderbilt Clinic, New York City, consulting surgeon, Hackensack General Hospital, Hackensack, New Jersey, Sharon Hospital, Sharon, Connecticut, and St. Joseph's Hospital, Far Rockaway, New York. Part One. *Deformities, Paralytic Disorders, Muscles, Tendons, Bursae, New Growths, Bones, Joints, Amputations.* 4°, cloth, 641 pp., with 520 illustrations and a color plate. *Part Two. Fractures, Dislocations, Sprains, Muscle and Tendon Injuries, Birth Injuries, Military Surgery.* 4°, cloth, 639 pp., with 543 illustrations. Philadelphia: J. B. Lippincott Company, 1945. $20.00.

This new treatise, a composite work of forty-three authorities in their particular fields, is primarily on surgical treatment, and therefore no attempt has been made to present the diagnostic problems or the etiology of the conditions in general. Selected lists of references are appended to each chapter. The text is well printed, with a good type, on good paper, but because of the necessity of using coated paper for the illustrations, the volumes are rather heavy for their size.

A Handbook on Diseases of Children: including dietetics and the common fevers. By Bruce Williamson, M.D. (Edin.), F.R.C.P. (Lond.), physician, Royal Northern and Prince of Wales hospitals, London, and physician (E.M.S.), Wellhouse Hospital, Barnet. Fourth edition. 12°, cloth, 388 pp., with 81 illustrations. Baltimore: The Williams and Wilkins Company, 1945. $4.50.

This fourth edition of a popular manual designed for medical students has been thoroughly revised, and recent advances in pediatrics have been introduced throughout the text. The colored plates, first introduced in the third edition, have been retained in this edition.

The Science and Art of Medicine: An inaugural lecture. By Sir Lionel Whitby, C.V.O., M.C., M.D. (Cantab.), F.R.C.P. (Lond.), D.P.H., Regius Professor of Physic, University of Cambridge. 12°, paper, 24 pp. New York: Cambridge University Press, The Macmillan Company, 1946. 50 cents.

In this inaugural address on assuming the office of Regius Professor of Physic, Cambridge University, Dr. Whitby briefly outlines the work of his predecessors, and selects for a brief exposition one aspect of scientific medicine, that of chemotherapy.

Pharmacology. By J. H. Gaddum, Sc.D., M.R.C.S., L.R.C.P., professor of pharmacology, University of Edinburgh. Oxford Medical Publications. Second edition. 8°, cloth, 460 pp., with 75 illustrations and 17 tables. New York: Oxford University Press, 1945. $6.00.

This second edition of a textbook written primarily for medical students has been brought up to date and improved in other ways. A limited number of references have been incorporated throughout the text. An appendix on the interpretation of chemical names should be found helpful. The material is well organized and well printed on a good paper with a large type and the manual should prove valuable as a short text on its subject.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, February 13

Friday, February 14

*9:00–10:00 a.m. Clinicopathological Conference. Drs. Chester S. Keefer and H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

Monday, February 17

*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

Tuesday, February 18

12:00 m.–1:00 p.m. Dermatological Service, Grand Rounds. Amphitheater, Dowling Building, Boston City Hospital.

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

Wednesday, February 19

*9:00–10:00 a.m. Pediatric Clinicopathological Conference. Drs. James M. Baty and H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

*11:00 a.m.–12:00 m. Medical Clinic. Amphitheater, Children's Hospital.

(*Notices continued on page xix*)

NOTICES (*Continued from page 222*)

*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.
*2:00-3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

October 11-May 14. Metropolitan State Hospital. [Page 398, issue of September 12.

February 7. American Board of Obstetrics and Gynecology. Page 44, issue of January 2.

February 9. National Conference on Medical Service. Page 956, issue of December 26.

February 11. Harvard Medical Society. Amphitheater, Peter Bent Brigham Hospital. 8:00 p.m.

February 12. Massachusetts Medico-Legal Society. Page 156, issue of January 23.

February 12. New England Dermatological Society. Page 190, issue of January 30.

February 13. The Clinical Importance of the Blood Type in Transfusions and in Obstetric Patients. Dr. Louis K. Diamond. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

February 26. Tufts Alpha Omega Alpha. Page 156, issue of January 23.

March 13. Cornell Medical Alumni Day. Page 156, issue of January 23.

April 28-May 2. American College of Physicians. Page 206, issue of August 8.

May 20-22. Massachusetts Medical Society. Annual meeting. Hotel Statler, Boston.

June 9-13. American Medical Association. Page 698, issue of November 7.

June 30-July 3. American Urological Association. Hotel Statler, Buffalo.

September 8-12. American Congress on Obstetrics and Gynecology. Page 636, issue of October 24.

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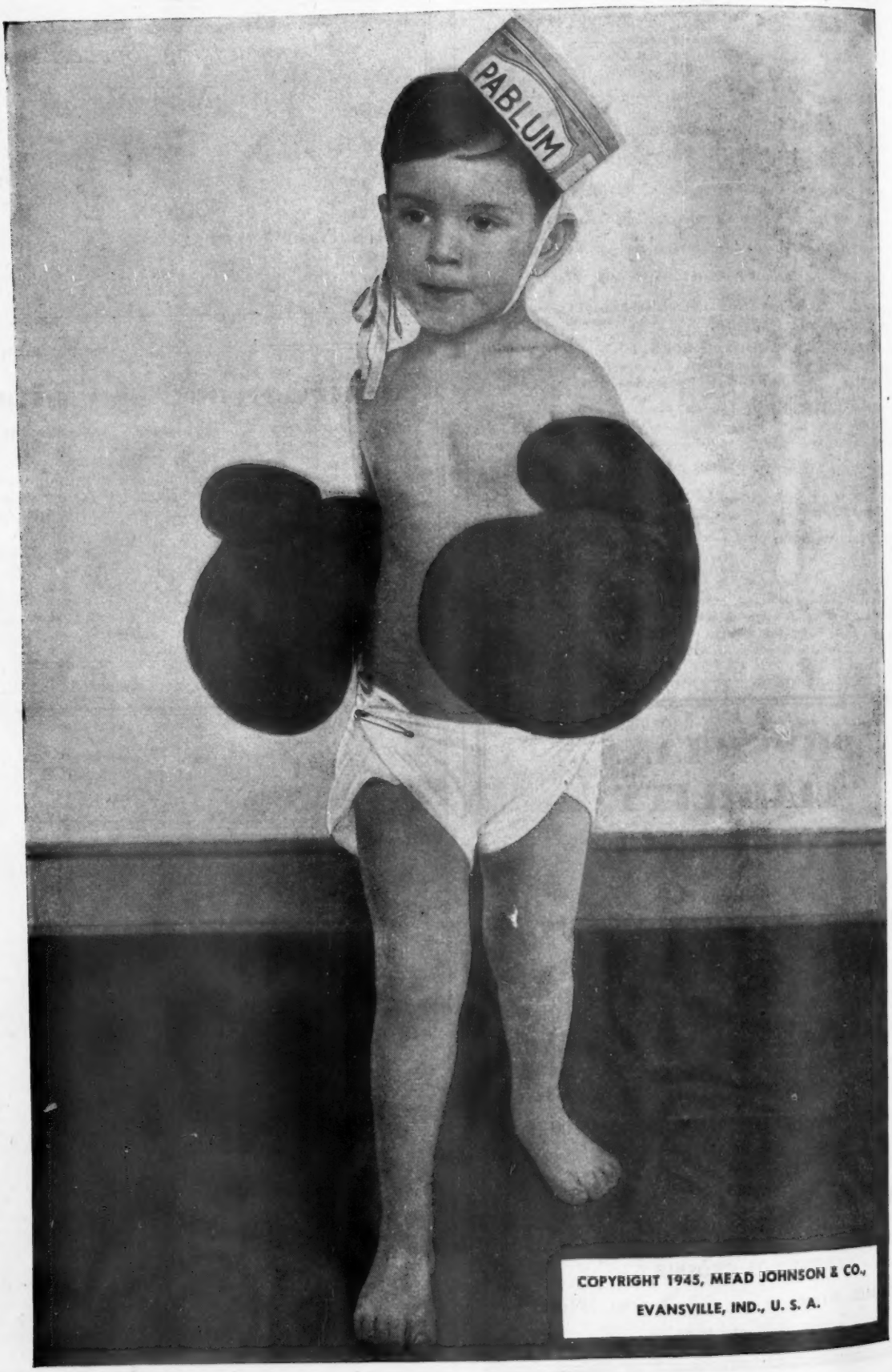
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